UI - 21261423
PMID- 11369016
DA - 20110522
LCOM- 20110523
IS - 0021-9150
VI - 156
IP - 1
DP - 2001 May
TI - Effect of intensive lipid-lowering strategy on low-density lipoprotein particle size in patients with type 2 diabetes mellitus.
PG - 109-16
AB - A preponderance of small dense LDL particles is strongly associated with the occurrence of atherosclerotic disease. Although several studies have documented an increased prevalence of small dense LDL particles in diabetes mellitus no data are available to show the effect of lipid-lowering treatment upon the improvement of LDL particle size. In the present study we examined the effect of lipid-lowering treatment, following an intensive lipid-lowering strategy for 30 weeks pursuing ADA recommended target lipid levels, on LDL particle size in 50 type 2 diabetic patients with moderate hyperlipidemia. At week 0, 24 patients (49%) were characterized by small dense LDL phenotype pattern B. After the treatment period a shift towards normal LDL particle size was observed in 17 patients but seven patients (29%) showed the more atherogenic LDL subclass pattern B. After treatment, plasma HDL-cholesterol was significantly lower (P<0.05) in these patients compared to those who had LDL subclass pattern A. Multivariate regression analysis revealed VLDL-cholesterol or triglycerides and HDL(3)-cholesterol as independent determinants for LDL particle size. Change in HDL(2)-cholesterol was an independent determinant for change in LDL particle size. In conclusion, a strategy of intensive lipid-lowering, with the intention to reduce triglyceride levels below 1.7 mmol/l, may be insufficient to ensure improvement in LDL size in all patients.
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FAU - Algra, A
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FAU - Erkelens, D W
AU - Erkelens DW
FAU - Banga, J D
AU - Banga JD
FAU - Jansen, H
AU - Jansen H
LA - eng
PT - Journal Article
CY - Ireland
TA - Atherosclerosis
JID - 0242543
RN - [illegible] Antilipemic Agents
RN - [illegible] Lipoproteins, HDL Cholesterol
RN - [illegible] Lipoproteins, LDL
RN - [illegible] Triglycerides
SB - IM
MH - Aged
MH - Antilipemic Agents/*therapeutic use
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/*drug therapy
MH - Female
MH - Human
MH - Hyperlipidemia/drug therapy etiology

MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL *blood *chemistry
MH - Male
MH - Middle Age
MH - Particle Size
MH - Support, Non-U.S. Gov't
MH - Triglycerides/blood
EDAT- 2001/05/23 10:00
MHDA- 2001/06/24 10:01
AID - S0021915000006420 [pii]
PST - ppublish
SO - Atherosclerosis 2001 May;155(1):209-16.

UI - 20544561
PMID- 11095462
DA - 20001129
DCOM- 20001214
IS - 0021-972X
VI - 85
IP - 11
DP - 2000 Nov
TI - Effect of insulin and sulfonylurea therapy, at the same level of blood glucose control, on low density lipoprotein subfractions in type 2 diabetic patients.
PG - 4188-92
AB - The aim of this study was to evaluate the effect of sc insulin (INS) compared with sulfonylurea (SUL) therapy, at the same level of blood glucose control, on the low density lipoprotein (LDL) subfraction profile in normolipidemic type 2 diabetic patients. Nine normolipidemic type 2 diabetic men (age, 56+/-3 yr; body mass index, 26.5+/-0.9 kg/m2; mean +/- SEM), after a 3-week wash-out period, were assigned to INS or SUL for 2 months in a randomized cross-over design. Doses were adjusted only during the first month and then were kept constant. At the end of the treatments, hemoglobin A1c, plasma lipids, LDL, and very low density lipoprotein (VLDL) subfraction profiles and plasma postheparin lipoprotein lipase and hepatic lipase (HL) activities were evaluated. Despite glucose control was similar at the end of both periods (hemoglobin A1c, 7.4+/-0.3% vs. 7.3+/-0.2%, INS vs. SUL), INS compared with SUL significantly reduced plasma triglyceride (0.9+/-0.1 vs. 1.1+/-0.1 mmol/L; P < 0.05). Although INS did not affect the LDL concentration, it induced a decrease in both the amount (59.0 +/- 9.8 vs. 76.1+/-16.8 mg/dL; P = NS) and the proportion (31.2+ -3.0% vs. 38.3+/-3.8%; P < 0.03) of small LDL. Moreover, the decrease in small LDL was positively related to the reduction of large VLDL (r = 0.67; P < 0.04) and HL (r = 0.69, P < 0.05) induced by insulin therapy. In conclusion, sc insulin therapy, independently of glucose control and even in the presence of quite low plasma triglyceride levels, is able to reduce small LDL particles in type 2 diabetic patients. This change is related to decreases in both HL activity and large VLDL particles.
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AU - Di Marino L
FAU - Annuzzi, G

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AU  - Annuzzi G
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FAU - Riccardi, G
AU  - Riccardi G
LA  - eng
PT  - Clinical Trial
PT  - Journal Article
PT  - Randomized Controlled Trial
CY  - UNITED STATES
TA  - J Clin Endocrinol Metab
JID - 0375362
RN  - 0 (Blood Glucose)
RN  - 0 (Hypoglycemic Agents)
RN  - 0 (Lipoproteins, HDL Cholesterol)
RN  - 0 (Lipoproteins, LDL)
RN  - 0 (Lipoproteins, VLDL)
RN  - 0 (Phospholipids)
RN  - 0 (Sulfonylurea Compounds)
RN  - 0 (Triglycerides)
RN  - 10238-21-8 (Glyburide)
RN  - 11061-68-0 (Insulin)
RN  - 57-88-5 (Cholesterol)
SB  - AIM
SB  - IM
MH  - Blood Glucose/*metabolism
MH  - Cholesterol/blood
MH  - Cross-Over Studies
MH  - Diabetes Mellitus, Non-Insulin-Dependent/*blood/*drug therapy
MH  - Drug Therapy, Combination
MH  - Glyburide/*therapeutic use
MH  - Human
MH  - Hypoglycemic Agents/*therapeutic use
MH  - Insulin/*therapeutic use
MH  - Lipoproteins, HDL Cholesterol/blood
MH  - Lipoproteins, LDL/*blood
MH  - Lipoproteins, VLDL/blood
MH  - Male
MH  - Middle Age
MH  - Phospholipids/blood
MH  - Postprandial Period
MH  - Regression Analysis
MH  - Sulfonylurea Compounds/*therapeutic use
MH  - Support, Non-U.S. Gov't
MH  - Triglycerides/blood
EDAT- 2000/11/30 11:00
MHDA- 2001/02/23 10:01
PST - ppublish
SO  - J Clin Endocrinol Metab 2000 Nov;85(11):4188-92.



UI  - [illegible]
PMID- [illegible]
DA  - [illegible]
DCOM- [illegible]
IS  - 0939-4753
VI  - 10
IP  - 4
DP  - 2000 Aug
TI  - Lipid and lipoprotein patterns in type 2 non-obese diabetic patients. Do
      Lp(a) levels decrease with improved glycemic control in these patients?
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PG - 264-8
AB - BACKGROUND AND AIM: In this study, we investigated the levels of apolipoprotein-AI (apo-AI), apolipoprotein (apo-B), triglyceride (TG), high-density-lipoprotein-cholesterol (HDL-C), low-density-lipoprotein-cholesterol (LDL-C), total cholesterol, lipoprotein(a) in a group of non-obese, type 2 diabetes mellitus patients with different types of treatment and a control group of non-obese, non-diabetic subjects. METHODS AND RESULTS: Patients were divided into three groups according to their treatment types: insulin, sulphonylurea and untreated groups. All groups were similar in sex, weights, known duration of diabetes and habits. Each group consisted of 30 subjects. There were no differences in apo-AI, apo-B and TG levels ($p > 0.05$), whereas HDL-C levels in the untreated group were significantly lower than those of the other groups ($p < 0.05$). Lp(a) levels in the untreated group were higher than in the other ($p < 0.05$). CONCLUSIONS: Gaining metabolic control in diabetes mellitus is crucial in pulling back lipid, lipoprotein and apolipoprotein levels to a desired level and in attenuating CAD (coronary artery disease) risk factors, and also in preventing CAD. Lp(a) levels in particular are decreased by insulin or sulfonylurea in non-obese patients with type 2 diabetes mellitus.
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FAU - Gultekin, F
AU - Gultekin F
FAU - Candan, F
AU - Candan F
LA - eng
PT - Journal Article
CY - ITALY
TA - Nutr Metab Cardiovasc Dis
JID - 9111474
RN - 0 (Apolipoprotein A-I)
RN - 0 (Apolipoproteins B)
RN - 0 (Blood Glucose)
RN - 0 (Hemoglobin A, Glycosylated)
RN - 0 (Lipids)
RN - 0 (Lipoprotein(a))
RN - 0 (Lipoproteins)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL Cholesterol)
RN - 0 (Sulfonylurea Compounds)
RN - 0 (Triglycerides)
RN - 11061-68-0 (Insulin)
RN - 21187-98-4 (Gliclazide)
RN - 57-88-5 (Cholesterol)
SB - IM
MH - Apolipoprotein A-I/blood
MH - Apolipoproteins B/blood
MH - Blood Glucose/metabolism
MH - Cholesterol/blood
MH - Comparative Study
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/drug therapy
MH - Female
MH - Gliclazide/therapeutic use
MH - Hemoglobin A, Glycosylated/analysis
MH - Human
MH - Insulin/therapeutic use
MH - Lipids/*blood
MH - Lipoprotein(a)/*blood
MH - Lipoproteins/*blood
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/blood
MH - Male
MH - Reference Values

MH - Sulfonylurea Compounds/therapeutic use
MH - Triglycerides/blood
EDAT- 2000/11/18 11:00
MHDA- 2001/05/03 10:01
PST - ppublish
SO - Nutr Metab Cardiovasc Dis 2000 Aug;10(4):204-8.

UI - 20217297
PMID- 10751747
DA - 20000531
DCOM- 20000531
LR - 20001218
IS - 1590-8952
VI - 10
IP - 2
DP - 2000 Mar-Apr
TI - Pravastatin compared to bezafibrate in the treatment of dyslipidemia in insulin-treated patients with type 2 diabetes mellitus.
PG - 82-7
AB - BACKGROUND: Both HMG-CoA reductase inhibitors and fibric acid derivates are used for the treatment of dyslipidemia in Type 2 diabetes patients. The aim of this study was to compare the lipid lowering effect of 40 mg pravastatin, a HMG-CoA reductase inhibitor, and 400 mg bezafibrate, a fibric acid derivate, on serum lipids, lipoproteins and lipoprotein composition in 45 (22 men and 23 women) dyslipidemic, insulin-treated Type 2 diabetes patients. METHOD: The study used a double-blind, cross-over design. RESULTS: Pravastatin treatment was more effective in reducing total cholesterol, LDL-cholesterol, LDL-triglycerides, LDL-ApoB and LDL/HDL-cholesterol ratio (all p<0.001 between groups) and total/HDL-cholesterol and ApoA1/LDL-ApoB ratios (both p<0.01) and always induced a decrease in LDL-cholesterol concentrations and LDL/HDL-cholesterol ratio irrespective of baseline triglyceride concentration. Bezafibrate was more effective in increasing HDL-cholesterol (p<0.01 between groups), ApoA1 lipoprotein and decreasing triglycerides (both p<0.001 between groups) but induced an increase in LDL-cholesterol concentration particularly in patients with baseline triglyceride concentrations exceeding 2.0 mmol/l. With bezafibrate treatment the LDL-cholesterol/LDL-ApoB ratio showed a tendency to rise, suggesting a change in the LDL particle composition to a less small and dense form, while pravastatin treatment induced a decrease in this ratio suggesting a change in the LDL particle to a more dense form. With pravastatin treatment a small rise in HbA(1c) was observed. CONCLUSION: Pravastatin treatment is superior in lowering cholesterol-enriched lipoprotein subpopulations and improving cardiovascular risk factors. Bezafibrate is more effective in raising HDL-cholesterol and alters LDL particle composition to a more favorable form.
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FAU - Donker, A J
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FAU - Heine, R J
AU - Heine RJ
LA - eng
PT - Clinical Trial

PT - Journal Article
PT - Randomized Controlled Trial
CY - ENGLAND
TA - Diabetes Metab Res Rev
JID - 1[illegible]
RN - [illegible] (Anticholesteremic Agents)
RN - [illegible] (Antilipemic Agents)
RN - [illegible] (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL Cholesterol)
RN - [illegible] (Lipoproteins, VLDL Cholesterol)
RN - [illegible] (Triglycerides)
RN - 11061-6[illegible]-[illegible] (Insulin)
RN - 41859-67-0 (Bezafibrate)
RN - 57-88-5 (Cholesterol)
RN - 81093-37-0 (Pravastatin)
SB - IM
MH - Adult
MH - Aged
MH - Anticholesteremic Agents/therapeutic use
MH - Antilipemic Agents/*therapeutic use
MH - Bezafibrate *therapeutic use
MH - Cholesterol blood
MH - Comparative Study
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*complications/*drug therapy
MH - Female
MH - Human
MH - Hyperlipidemia/blood/complications/*drug therapy
MH - Insulin/*therapeutic use
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/blood
MH - Lipoproteins, VLDL Cholesterol/blood
MH - Male
MH - Middle Age
MH - Pravastatin *therapeutic use
MH - Triglycerides/blood
EDAT- 2000/04/07 09:00
MHDA- 2000/06/03 09:00
AID - 10.1002/(SICI)1520-7560(200003/04)16:2<82::AID-DMRR89>3.0.CO;2-G [pii]
PST - ppublish
SO - Diabetes Metab Res Rev 2000 Mar-Apr;16(2):82-7.

UI - 20250719
PMID- 10821063
DA - 20000604
DCOM- 20000604
LR - 20061[illegible]
IS - 1[illegible]-16[illegible]X
VI - 16
IP - 2
DP - 2000 Jan-Mar
TI - The effect of glycaemic control on the prevalence and pattern of dyslipidaemia in Nigerian patients with newly diagnosed non insulin dependent diabetes mellitus.
PG - 27-33
AB - Dyslipidaemia (DL) is a common condition in patients with NIDDM, but its prevalence and the effect of glycaemic control on the disorder have only been scantily reported in Nigerians. The present study is therefore aimed at determining the effect of diabetic control on prevalence and pattern of DL in Nigerian patients with NIDDM. Thirty six diabetics were followed up for 24 weeks. Indices determined included anthropometric measurements, fasting (FBG) and two hour post prandial blood glucose (2 hours PPBG),

together with glycated haemoglobin (GHb) levels, and fasting lipids at presentation, 12 and after 24 weeks of treatment. The prevalence rates of raised total cholesterol, high density lipoprotein cholesterol (TC/HDL) ratio reduced HDL-cholesterol and mixed DL decreased significantly between 0-week and 24 weeks of treatment (57.1% vs 14.3% 50% vs 11.4% and 44% vs 12.2% respectively, P < 0.001 for each). The proportion of patient with elevated low-density lipoprotein-cholesterol also decreased significantly from 21.4% at 0-week to 8.8 after 24 weeks (P < 0.025). On the other hand, the prevalence of hypercholesterolaemia and hypertriglyceridaemia were not significantly changed between 0 and 24 weeks (P > 0.05). Patients with DL despite treatment were characterised by higher FBG at 24 weeks of treatment compared with normolipidaemic patients (P < 0.001). It is concluded from this study that improved glycaemic control reduced some dyslipidaemia, and may therefore suffice to correct them in some Nigerian patients with NIDDM.

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FAU - Akinlade, K S
AU - Akinlade KS
LA - eng
PT - Journal Article
CY - NIGERIA
TA - West Afr J Med
JID - 8501891
RN - 0 (Blood Glucose)
RN - 0 (Hemoglobin A, Glycosylated)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL Cholesterol)
RN - 0 (Triglycerides)
SB - IM
MH - Blood Glucose/analysis
MH - Case-Control Studies
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*complications/*prevention & control
MH - Female
MH - Follow-Up Studies
MH - Hemoglobin A, Glycosylated/metabolism
MH - Human
MH - Hyperlipidemia blood/*etiology
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/blood
MH - Male
MH - Middle Age
MH - Nigeria
MH - Prevalence
MH - Support, Non-U.S. Gov't
MH - Triglycerides/blood
EDAT- 2000/06/23 09:00
MHDA- 2000/06/10 09:01
PST - ppublish
SO - West Afr J Med 2000 Jan-Mar;19(1):27-33.

UI - 21012699
PMID- 11547808
DA - 19991117
DCOM- 19991117
LR - 20071218
IS - 0742-3071
VI - 16

IP - 10
DP - 1999 Oct
TI - The lipoprotein profile differs during insulin treatment alone and combination therapy with insulin and sulphonylureas in patients with Type 2 diabetes mellitus.
PG - 913-6
AB - AIMS: To study whether changes in endogenous insulin secretion at the same glycaemic control affect the plasma concentrations of lipoproteins in patients with Type 2 diabetes mellitus. METHODS: Fifteen patients, age 59+/-2 years (mean +/- SEM), body weight 86.3+/-3.0kg, body mass index 29.4+/-0.9 kg/m2 were treated with sulphonylurea and insulin in combination or with insulin alone in a randomized, double-blind, crossover study. All patients were treated with a multiple daily injection regimen with the addition of glibenclamide 10.5 mg daily or placebo tablets. RESULTS: During combination therapy, the dose of insulin was 25% less (P < 0.002) and there was a 29% increase in plasma C-peptide concentration (P = 0.01). Plasma levels of free insulin were not changed. Plasma levels of sex hormone-binding globulin (SHBG) and insulin-like growth factor-binding protein (IGFBP)-1 were lowered. There were no differences in the 24-h blood glucose profiles or HbA1c (6.0+/-0.2 vs. 6.3+/-0.2%; P = 0.16). Body weight was similar. There was a significant decrease in plasma LDL cholesterol (3.04+/-0.24 vs. 3.41+/-0.21 mmol/l; P = 0.04), apolipoprotein A1 and of lipoprotein(a) but an increase in VLDL-triglycerides (1.36+/-0.31 vs. 0.96+/-0.16 mmol/l; P = 0.02) during combination therapy. The ratio between LDL cholesterol and apolipoprotein B concentrations was significantly lower during combination therapy (P < 0.01). CONCLUSIONS: Combination therapy with insulin and sulphonylureas increases portal insulin supply and thereby alters liver lipoprotein metabolism when compared with insulin therapy alone.
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AU - Ottosson AM
FAU - Arnqvist, H J
AU - Arnqvist HJ
LA - eng
PT - Clinical Trial
PT - Journal Article
PT - Randomized Controlled Trial
CY - ENGLAND
TA - Diabet Med
JID - 8500845
RN - 0 (C-Peptide)
RN - 0 (Insulin-Like Growth Factor Binding Protein 1)
RN - 0 (Lipoproteins)
RN - 0 (Lipoproteins, LDL Cholesterol)
RN - 0 (Lipoproteins, VLDL)
RN - 0 (Sex Hormone-Binding Globulin)
RN - 0 (Sulfonylurea Compounds)
RN - 0 (Triglycerides)
RN - 11061-68-0 (Insulin)
RN - 67763-96-6 (Insulin-Like Growth Factor I)
SB - IM
MH - Aged
MH - C-Peptide/blood
MH - Cross-Over Studies
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/*drug therapy
MH - Double-Blind Method
MH - Female

MH - Human
MH - Insulin/administration & dosage/blood/*therapeutic use
MH - Insulin-Like Growth Factor I/analysis
MH - Insulin-Like Growth-Factor Binding Protein 1/blood
MH - Lipoproteins *blood
MH - Lipoproteins, LDL Cholesterol blood
MH - Lipoproteins, VLDL/blood
MH - Male
MH - Middle Age
MH - Sex Hormone-Binding Globulin/analysis
MH - Sulfonylurea Compounds/administration & dosage/*therapeutic use
MH - Support, Non-U.S. Gov't
MH - Triglycerides/blood
EDAT- 1999/11/05
MHDA- 1999/11/05 00:01
PST - ppublish
SO - Diabet Med 1999 Oct;16(10):820-6.

UI - 99441567
PMID- 10511896
DA - 19991026
DCOM- 19991026
LR - 20001218
IS - 0001-9355
VI - 54
IP - 4
DP - 1999 Aug
TI - Plasma lipoprotein (a) levels in Turkish NIDDM patients with and without vascular diabetic complications.
PG - 203-7
AB - OBJECTIVE: Plasma concentrations of lipoprotein (a) [Lp(a)], an independent risk factor for atherosclerosis, were measured in 59 non-insulin-dependent diabetes mellitus (NIDDM) patients with and without vascular complications, and 21 non-diabetic healthy subjects. RESULTS: The plasma log Lp(a) levels were found to be significantly increased in the NIDDM patients (1.40 +/- 0.36) compared with the healthy subjects (1.02 +/- 0.53; p < 0.05). Plasma Lp(a) levels in NIDDM patients with diabetic vascular complications (1.51 +/- 0.27) were significantly higher than those of the NIDDM patients without diabetic vascular complications (1.23 +/- 0.43) and healthy subjects (p < 0.05). There were significant correlations between plasma log Lp(a) levels and apolipoprotein B (apo B) in all NIDDM patients (r: 0.66, p < 0.05). No correlation was observed between Lp(a) levels and age, sex, duration of diabetes, fasting blood glucose, haemoglobin A1c, the mode of treatment, triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and apolipoprotein A1 levels in all patients. CONCLUSIONS: It was concluded that Lp(a) was a risk factor for angiopathy in NIDDM patients and the patients who have a high plasma Lp(a) concentration should be kept under strict glycaemic control
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AU - Sonmez M
FAU - Ulusoy, S

AU - Ulusoy S
FAU - Telatar, M
AU - Telatar M
LA - eng
PT - Journal Article
CY - BELGIUM
TA - Acta Cardiol
JID - 0370570
RN - 0 (Lipoprotein(a))
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL Cholesterol)
SB - IM
MH - Adult
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood
MH - Diabetic Angiopathies/blood
MH - Female
MH - Human
MH - Lipoprotein(a)/*blood
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/blood
MH - Male
MH - Middle Age
MH - Risk Factors
MH - Turkey
EDAT- 1999/10/08
MHDA- 1999/10/08 00:01
PST - ppublish
SO - Acta Cardiol 1999 Aug;54(4):203-7.

UI - 99367292
PMID- 10436249
DA - 20000405
DCOM- 20000405
LR - 20001114
IS - 0940-5429
VI - 36
IP - 1-2
DP - 1999 Jun
TI - The effect of gemfibrozil on lipid profile and glucose metabolism in hypertriglyceridaemic well-controlled non-insulin-dependent diabetic patients. For the Gemfibrozil Study Group.
PG - 27-33
AB - We assessed the efficacy of gemfibrozil therapy on lipid profile and glucose metabolism in a large cohort of (type 2) non-insulin-dependent diabetic patients. We enrolled 217 type 2 diabetic patients with plasma triglyceride concentrations equal to or above 2 mmol/l. 110 were randomized to gemfibrozil (600 mg twice daily) and 107 to placebo treatment in a double blind fashion. Each treatment was followed for 20 weeks. To assess postprandial glucose metabolism and insulin secretion, at time 0 and 20 weeks, a standard meal containing 12.5 g of proteins, 40.1 g of carbohydrate, 10 g of lipids was given. No differences in demographic characteristics were observed between patients randomized either to gemfibrozil or to placebo therapy. No differences were observed in total cholesterol and LDL-cholesterol concentration changes between the baseline observations and week 20 of both treatments. At variance, both treatments significantly increased HDL cholesterol. Gemfibrozil treatment significantly decreased plasma triglyceride concentration from 316+/-84 to 214+/-82 mg/dl (P < 0.001), whereas with placebo triglyceride levels increased from 318 + 95 to 380 + 217 mg/dl. No changes were observed in non-esterified fatty acid concentrations or in fasting plasma glucose concentrations, in HbA1c values, insulin and C-peptide concentrations. Gemfibrozil treatment: 1. significantly reduces circulating triglyceride

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      concentration; 2) does not significantly affect cholesterol concentration;
      3) does not worsen glucose metabolism.
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AU  - Miola M
FAU - Tiengo, A
AU  - Tiengo A
LA  - eng
PT  - Clinical Trial
PT  - Journal Article
PT  - Multicenter Study
PT  - Randomized Controlled Trial
CY  - GERMANY
TA  - Acta Diabetol
JID - 9200299
RN  - 0 (Antilipemic Agents)
RN  - 0 (Blood Glucose)
RN  - 0 (Fatty Acids, Nonesterified)
RN  - 0 (Hypoglycemic Agents)
RN  - 0 (Lipids)
RN  - 0 (Lipoproteins, HDL Cholesterol)
RN  - 0 (Lipoproteins, LDL Cholesterol)
RN  - 0 (Placebos)
RN  - 0 (Triglycerides)
RN  - 25812-30-0 (Gemfibrozil)
RN  - 57-88-5 (Cholesterol)
SB  - IM
MH  - Antilipemic Agents/*therapeutic use
MH  - Blood Glucose/drug effects/*metabolism
MH  - Cholesterol/blood
MH  - Diabetes Mellitus, Non-Insulin-Dependent/blood/complications/*drug therapy
MH  - Double-Blind Method
MH  - Fatty Acids, Nonesterified/blood
MH  - Female
MH  - Gemfibrozil/*therapeutic use
MH  - Human
MH  - Hypertriglyceridemia/blood/complications/*drug therapy
MH  - Hypoglycemic Agents/*therapeutic use
MH  - Italy
MH  - Lipids/*blood
MH  - Lipoproteins, HDL Cholesterol/blood
MH  - Lipoproteins, LDL Cholesterol/blood
MH  - Male
MH  - Middle Age
MH  - Placebos
MH  - Triglycerides/blood
EDAT- 1999/08/07
MHDA- 1999/08/07 00:01
AID - 9036/127.892 [pii]
PST - ppublish
SO  - Acta Diabetol 1999 Jun;36(1-2):27-33.

UI  - 99144496
PMID- 10024191
DA  - 19990225
DCOM- 19990225
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LR - 20001218
IS - 0026-0495
VI - 48
IP - 2
DP - 1999 Feb
TI - Long-lasting antidiabetic effect of a dipeptidyl peptidase IV-resistant analog of glucagon-like peptide-1.
PG - 252-8
AB - Glucagon-like peptide-1(7-37) (GLP-1) is the most potent insulinotropic hormone characterized thus far. Because its activity is preserved in non-insulin-dependent diabetes mellitus (NIDDM) patients, it is considered a potential new drug for the treatment of this disease. One limitation in its therapeutic use is a short half-life in vivo (5 minutes), due in part to a fast degradation by the endoprotease dipeptidylpeptidase IV (DPPIV). Recently, it was reported that GLP-1 became resistant to DPPIV when the alanine residue at position 8 was replaced by a glycine (GLP-1-Gly8). We report here that this change slightly decreased the affinity of the peptide for its receptor (IC50, 0.41 +/- 0.14 and 1.39 +/- 0.61 nmol/L for GLP-1 and GLP-1-Gly8, respectively) but did not change the efficiency to stimulate accumulation of intracellular cyclic adenosine monophosphate (cAMP) (EC50, 0.25 +/- 0.05 and 0.36 +/- 0.06 nmol/L for GLP-1 and GLP-1-Gly8, respectively). Second, we demonstrate for the first time that this mutant has an improved insulinotropic activity compared with the wild-type peptide when tested in vivo in an animal model of diabetes. A single injection of 0.1 nmol GLP-1-Gly8 in diabetic mice fed a high-fat diet can correct fasting hyperglycemia and glucose intolerance for several hours, whereas the activity of 1 nmol GLP-1 vanishes a few minutes after injection. These actions were correlated with increased insulin and decreased glucagon levels. Interestingly, normoglycemia was maintained over a period that was longer than the predicted peptide half-life, suggesting a yet undescribed long-term effect of GLP-1-Gly8. GLP-1-Gly8 thus has a markedly improved therapeutic potential compared with GLP-1, since it can be used at much lower doses and with a more flexible schedule of administration.
AD - Institute of Pharmacology and Toxicology, Lausanne, Switzerland.
FAU - Burcelin, R
AU - Burcelin R
FAU - Dolci, W
AU - Dolci W
FAU - Thorens, B
AU - Thorens B
LA - eng
PT - Journal Article
CY - UNITED STATES
TA - Metabolism
JID - 0375267
RN - 0 (Blood Glucose)
RN - 0 (Hypoglycemic Agents)
RN - 0 (Peptide Fragments)
RN - 0 (Protein Precursors)
RN - 11061-68-0 (Insulin)
RN - 89750-14-1 (glucagon-like peptide 1)
RN - 9007-92-5 (Glucagon)
RN - EC 3.4.14.5 (Antigens, CD26)
SB - IM
MH - Animal
MH - Antigens, CD26/*metabolism
MH - Area Under Curve
MH - Blood Glucose/metabolism
MH - Cells, Cultured
MH - Diet
MH - Glucagon/blood/metabolism/*pharmacology
MH - Glucose Tolerance Test
MH - Hypoglycemic Agents/metabolism/*pharmacology
MH - Insulin/blood

MH - Male
MH - Mice
MH - Mice, Inbred C57BL
MH - Peptide Fragments/metabolism/*pharmacology
MH - Protein Precursors/metabolism/*pharmacology
MH - Support, Non-U.S. Gov't
EDAT- 1999/02/19
MHDA- 1999/02/19 00:01
PST - ppublish
SO - Metabolism 1999 Feb;48(2):252-8.

UI - 99124988
PMID- 9918027
DA - 19990216
DCOM- 19990216
LR - 20001119
IS - 0077-8923
VI - 865
DP - 1998 Dec 11
TI - On the treatment of diabetes mellitus with glucagon-like peptide-1.
PG - 334-43
AB - As a therapeutic principle, the insulinotropic peptide, GLP-1, of the secretin-glucagon family of peptides, has turned out to possess some remarkably attractive properties, including the capability of normalizing blood glucose concentrations in patients with non-insulin-dependent diabetes mellitus and promoting satiety and reducing food intake in healthy volunteers. Because of rapid and extensive metabolization, the peptide is not immediately clinically applicable and, as a therapeutic principle, GLP-1 is still in its infancy. Some possible avenues for circumventing these difficulties are the development of DPP-IV-resistant analogs, the inhibition of DPP-IV, enhancement of GLP-1 secretion, GLP delivery systems using continuous subcutaneous infusion or buccal tablets, GLP-1 absorption, and orally active, stable analogs. It seems likely that one or more of these approaches could result in a clinically useful development program.
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AU - Deacon C
FAU - Toft-Nielsen, M B
AU - Toft-Nielsen MB
FAU - Bjerre-Knudsen, L
AU - Bjerre-Knudsen L
LA - eng
PT - Journal Article
PT - Review
PT - Review, Tutorial
CY - UNITED STATES
TA - Ann N Y Acad Sci
JID - 7506858
RN - 0 (Appetite Depressants)
RN - 0 (Hypoglycemic Agents)
RN - 0 (Peptide Fragments)
RN - 0 (Protein Precursors)
RN - 89750-14-1 (glucagon-like peptide 1)
RN - 9007-92-5 (Glucagon)
RN - EC 3.4.14.5 (Antigens, CD26)
SB - IM
MH - Administration, Oral
MH - Animal

MH - Antigens, CD26/metabolism
MH - *Appetite Depressants
MH - Diabetes Mellitus, Non-Insulin-Dependent/*drug therapy
MH - Glucagon/administration & dosage/*therapeutic use
MH - Human
MH - Hypoglycemic Agents/*therapeutic use
MH - Peptide Fragments/administration & dosage/*therapeutic use
MH - Protein Precursors/administration & dosage/*therapeutic use
RF - 37
EDAT- 1999/02/03
MHDA- 1999/02/03 00:01
PST - ppublish
SO - Ann N Y Acad Sci 1998 Dec 11;865:336-43.

UI - 98251119
PMID- 9589227
DA - 19980717
DCOM- 19980717
LR - 20011126
IS - 0149-5992
VI - 21
IP - 5
DP - 1998 May
TI - The effects of metformin on glycemic control and serum lipids in insulin-treated NIDDM patients with suboptimal metabolic control.
PG - 701-5
AB - OBJECTIVE: To test the hypothesis that metformin therapy, given as an adjunct to insulin therapy, improves metabolic control in insulin-treated NIDDM patients with suboptimal glycemic control. RESEARCH DESIGN AND METHODS: A total of 33 subjects with insulin-treated NIDDM were investigated; all had commenced insulin after secondary failure of antihyperglycemic agents. Two randomized double-blind placebo-controlled crossover studies were run. In study 1 (n = 19), insulin-treated subjects with suboptimal glycemic control received 12 weeks of metformin 1 g b.i.d. and 12 weeks of placebo. In study 2 (n = 14), subjects already established on adjunctive metformin/insulin therapy stopped the metformin component and received 12 weeks of metformin at their baseline dosage (range 1-2.5 g) and 12 weeks of equivalent placebo. Fasting plasma glucose, HbA1c, and serum lipids were measured at baseline and midway through and at the end of each treatment phase. The effect of 12 weeks of metformin treatment was compared with the effect of 12 weeks of placebo in each study and in both studies combined. RESULTS: In study 1, metformin treatment was associated with significant improvements in fasting plasma glucose (mean 12-week difference from placebo [95% CI]: 5.8 mmol/l [3.5-8.1], P < 0.001) and HbA1c (1.6% [0.9-2.4], P < 0.001). In study 2, metformin treatment was associated with significantly lower fasting plasma glucose (5.3 mmol/l [0.6-9.9], P = 0.029) and lower HbA1c (2.4% [1.0-3.8], P = 0.003) compared with those for placebo. Study 2 also showed metformin treatment to be associated with significantly lower total cholesterol than that for placebo (1.0 mmol/l [0.1-1.9], P = 0.032) and lower LDL cholesterol (1.0 mmol/l [0.1-1.8], P = 0.028). This significant difference in serum lipids seen in study 2 was not seen in study 1, but was present when both sets of data were combined (n = 33, mean total cholesterol difference at 12 weeks [95% CI]: 0.6 mmol/l [0.1-1.1], P = 0.016). Metformin had no significant effect on triglyceride, HDL cholesterol, weight, or blood pressure. Two subjects on metformin withdrew because of side effects. CONCLUSIONS: Metformin, when given as adjunctive therapy, was well tolerated and improved glycemic control and lipid concentrations in patients with insulin-treated NIDDM whose diabetes was poorly controlled. These improvements could be maintained over the long term.
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FAU - Atkinson, A C
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AU  - Burke J
FAU - Atkinson, S
AU  - Atkinson S
FAU - Johnston, D G
AU  - Johnston DG
FAU - Elkeles, R S
AU  - Elkeles RS
LA  - eng
PT  - Clinical Trial
PT  - Journal Article
PT  - Randomized Controlled Trial
CY  - UNITED STATES
TA  - Diabetes Care
JID - 7805975
RN  - 0 (Blood Glucose)
RN  - 0 (Hemoglobin A, Glycosylated)
RN  - 0 (Hypoglycemic Agents)
RN  - 0 (Lipids)
RN  - 0 (Lipoproteins, HDL Cholesterol)
RN  - 0 (Lipoproteins, LDL Cholesterol)
RN  - 0 (Triglycerides)
RN  - 11061-68-0 (Insulin)
RN  - 57-88-5 (Cholesterol)
RN  - 657-24-9 (Metformin)
SB  - IM
CIN - Diabetes Care. 1999 Mar;22(3):528. PMID: 10097944
MH  - Aged
MH  - Blood Glucose/*drug effects/metabolism
MH  - Blood Pressure/drug effects
MH  - Body Weight/drug effects
MH  - Cholesterol/blood
MH  - Cross-Over Studies
MH  - Data Interpretation, Statistical
MH  - Diabetes Mellitus, Non-Insulin-Dependent/blood/*drug therapy/metabolism
MH  - Diastole
MH  - Double-Blind Method
MH  - Fasting
MH  - Female
MH  - Glucose Tolerance Test
MH  - Hemoglobin A, Glycosylated/drug effects/metabolism
MH  - Human
MH  - Hyperglycemia/drug therapy/*prevention & control
MH  - Hypoglycemic Agents/*therapeutic use
MH  - Insulin/therapeutic use
MH  - Lipids/*blood
MH  - Lipoproteins, HDL Cholesterol/blood/drug effects
MH  - Lipoproteins, LDL Cholesterol/blood/drug effects
MH  - Male
MH  - Metformin/*therapeutic use
MH  - Middle Age
MH  - Support, Non-U.S. Gov't
MH  - Systole
MH  - Treatment Outcome
MH  - Triglycerides/blood
EDAT- 1999/05/21
MHDA- 1999/05/20 00:01
PST - ppublish
SO  - Diabetes Care 1998 May;21(5):701-5.
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UI - 98232818
PMID- 9571527
DA - 19980616
DCOM- 19980616
LR - 20001218
IS - 0149-5992
VI - 21
IP - 4
DP - 1998 Apr
TI - Treatment of hypercholesterolemia and combined hyperlipidemia with simvastatin and gemfibrozil in patients with NIDDM. A multicenter comparison study.
PG - 477-81
AB - OBJECTIVE: To compare the lipid-lowering efficacies of simvastatin and gemfibrozil in NIDDM patients with combined (mixed) hyperlipidemia (CHL) or isolated hypercholesterolemia (IHC). RESEARCH DESIGN AND METHODS: Patients with primary dyslipidemia and NIDDM were recruited for this double-blind, double-dummy comparison study from 10 Finnish centers. After a 4-week placebo run-in period, they were randomly assigned to simvastatin or gemfibrozil. The simvastatin group (n = 47) received 10 mg once nightly for 8 weeks, 20 mg for the next 8 weeks, and 40 mg for the third 8-week period. The gemfibrozil group (n = 49) received 600 mg twice daily throughout the 24 weeks. The lipid-lowering efficacies of both drugs were compared in all patients as well as separately in patients with CHL and IHC. RESULTS: In all patients, simvastatin reduced LDL and total cholesterol and the LDL-to-HDL cholesterol ratio more effectively, whereas gemfibrozil was more effective in elevating HDL cholesterol and decreasing triglyceride levels. The drug effects differed according to lipid phenotype at baseline. Simvastatin decreased LDL cholesterol levels by 30-40% in both phenotypes. Gemfibrozil caused a 15% reduction in LDL cholesterol in IHC but no change in CHL patients. Simvastatin produced 15-30% reductions in triglyceride levels in CHL but no change in IHC patients. Gemfibrozil caused reductions in triglycerides in CHL (50% and more) and in IHC (40%) patients, with 12-13% increases in HDL cholesterol in these groups. CONCLUSIONS: Simvastatin is useful in both CHL and IHC patients, whereas gemfibrozil can be used in patients with high triglyceride and low or normal LDL cholesterol levels.
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AU - Helve E
FAU - Maarsalo, E
AU - Maarsalo E
FAU - Pilkki, E
AU - Pilkki E
FAU - Saltevo, J
AU - Saltevo J
LA - eng
PT - Clinical Trial
PT - Journal Article
PT - Multicenter Study
PT - Randomized Controlled Trial
CY - UNITED STATES
TA - Diabetes Care
JID - 7805975
RN - 0 (Anticholesteremic Agents)
RN - 0 (Antilipemic Agents)
RN - 0 (Blood Glucose)
RN - 0 (Hemoglobin A, Glycosylated)
RN - 0 (Lipoproteins, HDL Cholesterol)

RN - 0 (Lipoproteins, LDL Cholesterol)
RN - 0 (Triglycerides)
RN - 25812-30-0 (Gemfibrozil)
RN - 57-88-5 (Cholesterol)
RN - 79902-63-9 (Simvastatin)
SB - IM
MH - Anticholesteremic Agents/*therapeutic use
MH - Antilipemic Agents/*therapeutic use
MH - Blood Glucose/drug effects
MH - Cholesterol/blood
MH - Comparative Study
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*complications
MH - Double-Blind Method
MH - Female
MH - Finland
MH - Gemfibrozil/*therapeutic use
MH - Hemoglobin A, Glycosylated/analysis
MH - Human
MH - Hypercholesterolemia/blood/complications/*drug therapy
MH - Hyperlipidemia/blood/complications/*drug therapy
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/blood
MH - Male
MH - Middle Age
MH - Simvastatin/*therapeutic use
MH - Support, Non-U.S. Gov't
MH - Time Factors
MH - Triglycerides/blood
EDAT- 1998/05/09
MHDA- 1998/05/09 00:01
PST - ppublish
SO - Diabetes Care 1998 Apr;21(4):477-81.

UI - 98192672
PMID- 9525995
DA - 19980423
DCOM- 19980423
LR - 20001219
IS - 0021-9738
VI - 101
IP - 7
DP - 1998 Apr 1
TI - Exendin(9-39)amide is an antagonist of glucagon-like peptide-1(7-36)amide in humans.
PG - 1421-30
AB - The gastrointestinal hormone, glucagon-like peptide-1(7-36)amide (GLP-1) is released after a meal. The potency of synthetic GLP-1 in stimulating insulin secretion and in inhibiting glucagon secretion indicates the putative physiological function of GLP-1. In vitro, the nonmammalian peptide, exendin(9-39)amide [ex(9-39)NH2], is a specific and competitive antagonist of GLP-1. This in vivo study examined the efficacy of ex(9-39)NH2 as an antagonist of exogenous GLP-1 and the physiological role of endogenous GLP-1. Six healthy volunteers underwent 10 experiments in random order. In each experiment, a 30-min period of euglycemia was followed by an intravenous infusion of glucose for 150 min that established a stable hyperglycemia of 8 mmol/liter. There was a concomitant intravenous infusion of one of the following: (1) saline, (2) GLP-1 (for 60 min at 0.8 pmol . kg-1 . min-1 that established physiological postprandial plasma levels, and for another 60 min at 0.9 pmol . kg-1 . min-1 to induce supraphysiological plasma levels), (3-5) ex(9-39)NH2 at 30, 60, or 300 pmol . kg-1 . min-1 + GLP-1, (6-8) ex(9-39)NH2 at 30, 60, or 300 pmol . kg-1 . min-1 + saline, (9 and 10) GIP

(glucose-dependent insulinotropic peptide; for 60 min at 0.8 pmol . kg-1 . min-1, with saline or ex(9-39)NH2 at 300 pmol . kg-1 . min-1). Each volunteer received each of these concomitant infusions on separate days. ex(9-39)NH2 dose-dependently reduced the insulinotropic action of GLP-1 with the inhibitory effect declining with increasing doses of GLP-1. ex(9-39)NH2 at 300 pmol . kg-1 . min-1 blocked the insulinotropic effect of physiological doses of GLP-1 and completely antagonized the glucagonostatic effect at both doses of GLP-1. Given alone, this load of ex(9-39)NH2 increased plasma glucagon levels during euglycemia and hyperglycemia. It had no effect on plasma levels of insulin during euglycemia but decreased plasma insulin during hyperglycemia. ex(9-39)NH2 did not alter GIP-stimulated insulin secretion. These data indicate that in humans, ex(9-39)NH2 is a potent GLP-1 antagonist without any agonistic properties. The pancreatic A cell is under a tonic inhibitory control of GLP-1. At hyperglycemia, the B cell is under a tonic stimulatory control of GLP-1.

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AU - Leicht P
FAU - Arnold, R
AU - Arnold R
FAU - Goke, B
AU - Goke B
FAU - Katschinski, M
AU - Katschinski M
LA - eng
PT - Clinical Trial
PT - Journal Article
PT - Randomized Controlled Trial
CY - UNITED STATES
TA - J Clin Invest
JID - 7802877
RN - 0 (C-Peptide)
RN - 0 (Peptide Fragments)
RN - 0 (Protein Precursors)
RN - 0 (Receptors, Glucagon)
RN - 0 (exendin (9-39) amide)
RN - 0 (glucagon-like peptide receptor)
RN - 11061-68-0 (Insulin)
RN - 50-99-7 (Glucose)
RN - 89750-14-1 (glucagon-like peptide 1)
RN - 9007-92-5 (Glucagon)
SB - AIM
SB - IM
MH - Adult
MH - C-Peptide/blood
MH - Glucagon/*antagonists & inhibitors/blood
MH - Glucose/metabolism
MH - Human
MH - Insulin/blood
MH - Male
MH - Peptide Fragments/*antagonists & inhibitors/blood/*pharmacology
MH - Protein Precursors/*antagonists & inhibitors/blood
MH - Receptors, Glucagon/*antagonists & inhibitors
MH - Support, Non-U.S. Gov't
MH - Time Factors
EDAT- 1996/04/29
MHDA- 1996/04/29 00:01
PST - ppublish

SO - J Clin Invest 1998 Apr 1;101(7):1421-30.

UI - 98159295
PMID- 9525146
DA - 19971031
DCOM- 19971031
LR - 20001218
IS - 0021-9738
VI - 33
IP - 10
DP - 1997 Oct
TI - Glucagon-like peptide-1 structure, function and potential use for NIDDM.
PG - 694-5
AB - Basic research on the cellular mechanisms that control the expression of the gene encoding glucagon has led to the discovery of proglucagon. This precursor is processed by tissue-specific proteolysis to produce glucagon in pancreatic alpha-cells and a glucagon-like peptide-1 (GLP-1) in the intestine. GLP-1 is a hormone that is released by intestinal cells into the circulation in response to food intake. GLP-1 and gastric inhibitory peptide (GIP) which has also been termed glucose-dependent insulinotropic peptide appear to account for most of the incretin effect in the augmentation of glucose-stimulated insulin secretion. These two hormones have specific beta-cell receptors that are coupled to GTP binding proteins to induce production of cyclic AMP and activation of cyclic AMP-dependent protein kinase. It is proposed that at least one factor contributing to the pathogenesis of non-insulin-dependent diabetes mellitus (NIDDM) is desensitization of the GLP-1 receptor on beta-cells. At pharmacological doses, infusion of GLP-1, but not of GLP, can improve and enhance postprandial insulin response in NIDDM patients. Agonists of GLP-1 receptor have been proposed as new potential therapeutic agents in NIDDM patients. The observations that GLP-1 induces both secretion and production of insulin, and that its activities are mainly glucose-dependent, led to the suggestion that GLP-1 may present a unique advantage over sulfonylurea drugs in the treatment of NIDDM.
AD - Department of Internal Medicine C, Barzilai Medical Center, Ashkelon, Israel.
FAU - Gefel, D
AU - Gefel D
FAU - Barg, Y
AU - Barg Y
FAU - Dimlichman, R
AU - Dimlichman R
LA - eng
PT - Journal Article
PT - Review
PT - Review, Tutorial
CY - ISRAEL
TA - Isr J Med Sci
JID - 0013105
RN - (Peptide Fragments)
RN - (Protein Precursors)
RN - (Receptors, Glucagon)
RN - (glucagon-like peptide receptor
RN - 11061-68-0 (Insulin)
RN - 89750-14-1 (glucagon-like peptide 1)
RN - 9007-92-5 (Glucagon)
SB - IM
MH - Diabetes Mellitus, Non-Insulin-Dependent/*drug therapy/*genetics/metabolism
MH - Gastric Emptying/drug effects
MH - Glucagon/chemistry/*physiology/*therapeutic use
MH - Human

MH - Insulin/secretion
MH - Insulin Resistance
MH - Islets of Langerhans/*drug effects
MH - Peptide Fragments/chemistry *physiology *therapeutic use
MH - Protein Precursors/chemistry *physiology *therapeutic use
MH - Receptors, Glucagon/*agonists
RF - 23
EDAT- 1997/12/16
MHDA- 1997/12/16 00:01
PST - ppublish
SO - Isr J Med Sci 1997 Oct;33(10):690-5.

UI - 97428447
PMID- 9342797
DA - 19971118
DCOM- 19971118
LR - 20001118
IS - 0149-5992
VI - 20
IP - 9
DP - 1997 Sep
TI - Lack of change of lipoprotein(a) levels by the optimization of glycemic control with insulin therapy in NIDDM patients.
PG - 1459-61
AB - OBJECTIVE: To evaluate the effect of glycemic control improvement with insulin therapy on lipoprotein(a) [Lp(a)] levels in patients with NIDDM. RESEARCH DESIGN AND METHODS: We performed a longitudinal study in a tertiary referral center to compare lipid and Lp(a) levels before and after 3 months of insulin therapy in 60 poorly controlled NIDDM patients (32 men, 28 women). Patients previously treated with oral hypoglycemic agents (n = 50) received one to two insulin doses, and those previously treated with insulin (n = 10) received multiple insulin doses. Lp(a) levels were measured by the Terumo method. Differences between the two periods were assessed by the paired t test and Wilcoxon's test. RESULTS: After 3 months of insulin therapy, HbA1c decreased from 9.6 +/- 1.9 to 6.0 +/- 1.4% (P < 0.0005) in all patients and from 9.1 +/- 2.1 to 6.1 +/- 2.9% (P < 0.05) in patients under multiple insulin doses, being < or = 6.0% in 59% of patients. Total triglyceride and VLDL cholesterol levels decreased (P < 0.01) and HDL cholesterol increased significantly (P < 0.0005). However, no changes in Lp(a) levels were observed in all patients (25.3 +/- 25.0 vs 25.7 +/- 27.2% mg/dl) and in patients with baseline Lp(a) levels above (63.5 +/- 18.5 vs. 65.1 +/- 23.1 mg/dl) or below 30 mg/dl (11.5 +/- 7.5 vs. 11.9 +/- 7.3 mg/dl). In addition, patients reaching HbA1c levels < or = 6.0% or > 6.0% presented similar Lp(a) levels (26.0 +/- 29.1 vs 25.3 +/- 25.3 mg/dl). Moreover, no correlations were observed between changes in Lp(a) levels and in the glycemic control parameters. CONCLUSIONS: This study shows that the improvement of glycemic control by insulin therapy does not influence plasma Lp(a) levels, measured by the Terumo method, in NIDDM patients, independently of baseline values and the degree of glycemic control reached.
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AU - Ordonez-Llanos J
FAU - Bonet, R
AU - Bonet R
FAU - Rigla, M
AU - Rigla M

FAU - Castelli, A
AU - Castelli A
FAU - Bayer, L
AU - Bayer L
FAU - de Leiva, A
AU - de Leiva A
LA - eng
PT - Journal Article
CY - UNITED STATES
TA - Diabetes Care
JID - 7805975
RN - 0 (Hemoglobin A, Glycosylated)
RN - 0 (Hypoglycemic Agents)
RN - 0 (Lipids)
RN - 0 (Lipoprotein(a))
RN - 11061-68-0 (Insulin)
SB - IM
MH - Aged
MH - Comparative Study
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*drug therapy/metabolism
MH - Female
MH - Hemoglobin A, Glycosylated/analysis/drug effects/metabolism
MH - Human
MH - Hypoglycemic Agents/*therapeutic use
MH - Insulin/*therapeutic use
MH - Lipids/blood
MH - Lipoprotein(a)/*blood/drug effects/metabolism
MH - Longitudinal Studies
MH - Male
MH - Middle Age
MH - Time Factors
EDAT- 1997/09/01
MHDA- 1997/09/01 00:01
PST - ppublish
SO - Diabetes Care 1997 Sep;20(9):1459-61.

UI - 97444139
PMID- 9200657
DA - 19970716
DCOM- 19970716
LR - 20021101
IS - 0012-1797
VI - 46
IP - 7
DP - 1997 Jul
TI - Optimization of glycemic control by insulin therapy decreases the proportion of small dense LDL particles in diabetic patients.
PG - 1207-13
AB - Small dense LDL particles (B phenotype) are considered to be more atherogenic than large buoyant LDL particles. The influence of glycemic control on LDL particle size and density is still under debate. The aim of this study was to determine LDL subfraction phenotype in both IDDM and NIDDM patients in poor glycemic control compared with that of respective matched control groups. In addition, we evaluated the effect of a 3-month period of optimized glycemic control on this parameter. Thirty-seven IDDM patients and 33 NIDDM patients, together with two respective age-, sex-, and BMI-matched control groups were studied. Non-A phenotype prevalence in IDDM patients before (19%) and after blood glucose optimization (11%) was similar to that of their control group (12%). However, NIDDM patients displayed a higher proportion of the non-A phenotype (51%) than did the control group (29%), but it became closer (30%, P < 0.05) after glycemic control improved. All subjects with non-A phenotype that changed to A

phenotype showed triglyceride levels below 1.63 mmol/l and a greater decrease in HbA1c than did subjects whose phenotype did not change (4.9 +/- 1.5 vs. 3.1 +/- 1.4%, P < 0.05). A higher proportion of small dense LDL was observed in NIDDM women than in nondiabetic women (LDL5 10.0 +/- 4.9 vs. 6.3 +/- 1.5%, LDL6 6.1 +/- 2.2 vs. 4.2 +/- 0.8%, P < 0.05) during both stages of glycemic control, but no differences were observed between NIDDM and nondiabetic men. In conclusion, these findings provide new evidence for the relevance of near-normal glycemic control in the prevention of macrovascular disease and could contribute to an explanation of the loss of protection for cardiovascular disease in diabetic women.

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FAU - Hayes, A
AU - Hayes A
FAU - Homs, F
AU - Homs F
FAU - Perez, A
AU - Perez A
LA - eng
PT - Journal Article
CY - UNITED STATES
TA - Diabetes
JID - 0372763
RN - 0 (Blood Glucose)
RN - 0 (Hypoglycemic Agents)
RN - 0 (Lipids)
RN - 0 (Lipoproteins, LDL)
RN - 11061-68-0 (Insulin)
SB - AIM
SB - IM
MH - Adolescent
MH - Adult
MH - Aged
MH - Aged, 80 and over
MH - Blood Glucose/analysis/drug effects/metabolism
MH - Comparative Study
MH - Diabetes Mellitus, Insulin-Dependent/*blood/drug therapy/physiopathology
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/drug therapy/physiopathology
MH - Female
MH - Human
MH - Hypoglycemic Agents/*therapeutic use
MH - Insulin/*therapeutic use
MH - Lipids/blood/metabolism
MH - Lipoproteins, LDL/*blood/drug effects
MH - Male
MH - Middle Age
MH - Support, Non-U.S. Gov't
EDAT- 1997/07/01
MHDA- 1997/07/01 00:01
PST - ppublish
SO - Diabetes 1997 Jul;46(7):1207-13.

UI - 97387144
PMID- 9240117
DA - 19970815

DCOM- 19971015
LR - 20031218
IS - 0012-186X
VI - 40
IP - 7
DP - 1997 Jul
TI - Short-term oestrogen replacement therapy improves insulin resistance, lipids and fibrinolysis in postmenopausal women with NIDDM.
PG - 843-9
AB - Oestrogen replacement therapy is associated with a decreased risk of cardiovascular disease in postmenopausal women. Patients with non-insulin-dependent diabetes mellitus (NIDDM) have an increased cardiovascular risk. However, oestrogen replacement therapy is only reluctantly prescribed for patients with NIDDM. In a double blind randomized placebo controlled trial we assessed the effect of oral 17 beta-estradiol during 6 weeks in 40 postmenopausal women with NIDDM. Glycated haemoglobin (HbA1c), insulin sensitivity, suppressibility of hepatic glucose production, lipoprotein profile and parameters of fibrinolysis were determined. The oestrogen treated group demonstrated a significant decrease of HbA1c and in the normotriglyceridaemic group a significantly increased suppression of hepatic glucose production by insulin. Whole body glucose uptake and concentrations of non-esterified fatty acids did not change. LDL-cholesterol- and apolipoprotein B levels decreased, and HDL-cholesterol, its subfraction HDL2-cholesterol and apolipoprotein A1 increased. The plasma triglyceride level remained similar in both groups. Both the concentration of plasminogen activator inhibitor-1 antigen and its active subfraction decreased. Tissue type plasminogen activator activity increased significantly only in the normotriglyceridaemic group. Oestrogen replacement therapy improves insulin sensitivity in liver, glycaemic control, lipoprotein profile and fibrinolysis in postmenopausal women with NIDDM. For a definite answer as to whether oestrogens can be more liberally used in NIDDM patients, long term studies including the effect of progestogens are necessary.
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FAU - Kluft, C
AU - Kluft C
FAU - Krans, H M
AU - Krans HM
LA - eng
PT - Clinical Trial
PT - Journal Article
PT - Randomized Controlled Trial
CY - GERMANY
TA - Diabetologia
CID - 9006777
RN - 1 (C-Peptide)
RN - 1 (Fatty Acids, Nonesterified)
RN - 1 (Hemoglobin A, Glycosylated)
RN - 0 (Lipids)
RN - 0 (Lipoproteins)
RN - 0 (Plasminogen Activator Inhibitor 1)
RN - 1 (Triglycerides)
RN - 50-28-2 (Estradiol)
RN - 57-88-5 (Cholesterol)
RN - EC 3.4.21.68 (Tissue Plasminogen Activator)
SB - IM
MH - C-Peptide/*blood
MH - Cholesterol/blood

MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*drug therapy/*physiopathology
MH - Double-Blind Method
MH - Estradiol *therapeutic use
MH - *Estrogen Replacement Therapy
MH - Fatty Acids, Nonesterified/blood
MH - Female
MH - Fibrinolysis/*drug effects
MH - Hemoglobin A, Glycosylated/analysis
MH - Human
MH - *Insulin Resistance
MH - Lipids/*blood
MH - Lipoproteins/blood
MH - Middle Age
MH - Plasminogen Activator Inhibitor 1/blood
MH - Postmenopause
MH - Support, Non-U.S. Gov't
MH - Tissue Plasminogen Activator/blood
MH - Triglycerides/*blood
EDAT- 1997/07/01
MHDA- 1997/07/01 00:01
PST - ppublish
SO - Diabetologia 1997 Jul;40(7):843-9.

UI - 97283432
PMID- 9051204
DA - 19970709
DCOM- 19970709
LR - 20061219
IS - 0021-9150
VI - 128
IP - 1
DP - 1997 Jan 3
TI - Plasma lipoproteins and incidence of non-insulin-dependent diabetes mellitus in Pima Indians: protective effect of HDL cholesterol in women.
PG - 113-9
AB - The role of plasma lipoproteins in the development of non-insulin-dependent diabetes mellitus (NIDDM) was studied in 787 non-diabetic (2-h glucose < 11.1 mmol/l) Pima Indians (265 men and 522 women). Subjects were followed for a mean of 9.8 (range 1.8-16.4) years, during which 241 (76 men and 165 women) developed NIDDM. In men and women, very-low-density lipoprotein (VLDL) cholesterol, VLDL triglyceride, low-density lipoprotein triglyceride and total triglyceride, controlled for age, predicted NIDDM (P < 0.01 for each). These effects diminished when controlled for age, sex, body mass index, systolic blood pressure and 2-h glucose. However, high-density lipoprotein (HDL) cholesterol, controlled for age, body mass index, systolic blood pressure and 2-h glucose, was a significant protective factor for NIDDM in women (hazard rate ratio (HRR) = 0.35, 95% CI (0.23-0.54), P < 0.001, 90th compared with 10th percentile) but not in men (HRR = 1.04, 95% CI (0.53-2.05), P = 0.919). This association remained significant in women when controlled for fasting or 2-h plasma insulin concentrations, other estimates of insulin resistance or alcohol consumption. The protective effect of HDL cholesterol was similar among women with normal (2-h glucose < 7.8 mmol/l) or impaired (7.8 mmol/l < or = 2-h glucose < 11.1 mmol/l) glucose tolerance at baseline. These results indicate that lipoprotein disorders are an early accompaniment of the abnormalities that lead to NIDDM.
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FAU - Pettitt, D J
AU - Pettitt DJ
FAU - Knowler, W C
AU - Knowler WC
LA - eng
PT - Journal Article
CY - IRELAND
TA - Atherosclerosis
JID - 0242543
RN - 0 (Blood Glucose)
RN - 0 (Lipoproteins)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL)
RN - 0 (Lipoproteins, VLDL)
RN - 0 (Lipoproteins, VLDL Cholesterol)
RN - 0 (Triglycerides)
RN - 0 (low density lipoprotein triglyceride)
RN - 0 (very low density lipoprotein triglyceride)
RN - 11061-68-0 (Insulin)
SB - IM
MH - Adult
MH - Arizona
MH - Blood Glucose/analysis
MH - Blood Pressure
MH - Body Mass Index
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*ethnology
MH - Female
MH - Human
MH - *Indians, North American
MH - Insulin blood
MH - Insulin Resistance
MH - Lipoproteins/*blood
MH - Lipoproteins, HDL Cholesterol/*blood
MH - Lipoproteins, LDL/blood
MH - Lipoproteins, VLDL/blood
MH - Lipoproteins, VLDL Cholesterol/blood
MH - Male
MH - Proportional Hazards Models
MH - Risk Factors
MH - Triglycerides/blood
EDAT- 1997/01/03
MHDA- 1997/01/03 00:01
AID - S0021915096059783 [pii]
PST - ppublish
SO - Atherosclerosis 1997 Jan 3;128(1):113-9.

UI - 96119712
PMID- 8419614
DA - 19930205
DCOM- 19940205
LR - 20071115
IS - 0236-5383

VI - 48
IP - 3
DP - 1997
TI - Treatment possibility of hypercholesterolaemia associated with hypertriglyceridaemia.
PG - 359-67
AB - Thirty patients were investigated with hyperlipoproteinaemia, 15 patients with non-insulin dependent diabetes mellitus (NIDDM) and 15 with primary hyperlipoproteinaemia. The patients took 250 mg acipimox (5-metyl-pyrazine-carboxylic acid 4-oxide) 3 times per day for 2 months. Serum examinations were performed before and after 1 and 2 months of acipimox administration. After treatment the cholesterol and triglyceride levels decreased in both groups. Patients with NIDDM had 11% increase of high density lipoprotein-cholesterol (HDL-C) level at the end of the first, and 18% increase at the end of the second month, while patients with primary hyperlipoproteinaemia did not change significantly. The low density lipoprotein (LDL) level did not change significantly in either groups of patients. The apolipoprotein A 1 (apo A 1) levels increased significantly during the second month of acipimox administration. Uric acid levels decreased in both groups, but significant change could be detected mainly in the NIDDM group. Serum glucose level did not change in the non-diabetic patients, while it decreased significantly in the NIDDM group.
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AU - Balogh Z
FAU - Boda, J
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AU - Kovacs P
FAU - Karpati, L
AU - Karpati L
FAU - Szabo, J
AU - Szabo J
FAU - Leovey, A
AU - Leovey A
LA - eng
PT - Journal Article
CY - HUNGARY
TA - Acta Biol Hung
JID - 8404358
RN - 0 (Antilipemic Agents)
RN - 0 (Apolipoprotein A-I)
RN - 0 (Blood Glucose)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL)
RN - 0 (Pyrazines)
RN - 0 (Triglycerides)
RN - 51037-30-0 (acipimox)
RN - 57-88-5 (Cholesterol)
RN - 69-93-2 (Uric Acid)
SB - IM
MH - Antilipemic Agents/*therapeutic use
MH - Apolipoprotein A-I/blood
MH - Blood Glucose/metabolism
MH - Cholesterol/blood
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood/*drug therapy
MH - Female
MH - Human
MH - Hypercholesterolemia/blood/*complications/*drug therapy
MH - Hyperlipoproteinemia/blood/*drug therapy
MH - Hypertriglyceridemia/blood/*complications/*drug therapy

MH - Lipoproteins, HDL Cholesterol blood
MH - Lipoproteins, LDL blood
MH - Male
MH - Middle Age
MH - Pyrazines/*therapeutic use
MH - Time Factors
MH - Triglycerides/therapeutic use
MH - Uric Acid/blood
EDAT- 1997/12/24
MHDA- 1997/12/24 00:01
PST - ppublish
SO - Acta Biol Hung 1997;48(3):359-67.

UI - 97064830
PMID- 8904990
DA - 19970224
DCOM- 19970224
LR - 20001219
IS - 0140-5992
VI - 19
IP - 11
DP - 1996 Nov
TI - The antidiabetogenic effect of GLP-1 is maintained during a 7-day treatment period and improves diabetic dyslipoproteinemia in NIDDM patients.
PG - 1200-6
AB - OBJECTIVE: To investigate the long-term antidiabetogenic effect of glucagon-like peptide 1 (GLP-1) and its influence on diabetic dyslipoproteinemia, patients with NIDDM were treated with GLP-1 subcutaneously for 1 week. RESEARCH DESIGN AND METHODS: Twelve patients participated in the study. The 1st week of the study, all of them were on intensive insulin treatment and from day 8, four were randomized to a control group continuing with insulin, and eight to a treatment group where GLP-1 was given at meals together with regular insulin from day 8 to 12. On days 13 and 14, they were only given GLP-1 at meals. NPH insulin at bedtime was given throughout the study. RESULTS: In the GLP-1-treated patients, the doses of regular insulin, given to keep a satisfactory blood glucose control, were reduced compared with treatment with insulin only. GLP-1 virtually inhibited the early increase in blood glucose after the meals, whereas an increase of approximately 2 mmol was seen during an optimized insulin treatment. In agreement with the short half-life of the peptide, 2-h postprandial plasma insulin levels were significantly decreased both at day 12 and 14, suggesting that there was not enough GLP-1 left to stimulate endogenous insulin release and compensate for the decrease in the dose of exogenous insulin. Therefore, the effect of GLP-1 was lost before the next meal, resulting in increased preprandial blood glucose values at lunch and dinner. The concentration of VLDL triglycerides decreased already during the 1st week. This decrease persisted during the 2nd week when GLP-1 was included in the treatment. No changes were observed in the levels of LDL and HDL cholesterol. The LDL particle diameter increased from a mean of 22.3 to 22.6 nm ($P < 0.01$) in response to insulin treatment. A further increment to 22.9 nm ($P < 0.05$) was seen after GLP-1 treatment. The LDL particle size did not change in the control group. Lipoprotein lipase activity was decreased by 27% and hepatic lipase was reduced by 15% in the GLP-1-treated group. CONCLUSIONS: We confirm the antidiabetogenic effect of GLP-1 in NIDDM patients. This effect was maintained during 7 days, which implies that the patients did not develop tolerance during this treatment period. Intensive insulin treatment, leading to normotriglyceridemia, increased the mean LDL particle diameter, which is likely to lower the risk of future coronary heart disease in patients with NIDDM. Furthermore, an additive effect of GLP-1 is indicated. Hence, this study gives additional evidence that GLP-1

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      may be useful as an agent for treating NIDDM.
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FAU - Vignati, L
AU  - Vignati L
FAU - Efendic, S
AU  - Efendic S
LA  - eng
PT  - Clinical Trial
PT  - Journal Article
PT  - Randomized Controlled Trial
CY  - UNITED STATES
TA  - Diabetes Care
JID - 7805975
RN  - 0 (Blood Glucose)
RN  - 0 (C-Peptide)
RN  - 0 (Hemoglobin A, Glycosylated)
RN  - 0 (Hypoglycemic Agents)
RN  - 0 (Lipoproteins, HDL Cholesterol)
RN  - 0 (Lipoproteins, LDL Cholesterol)
RN  - 0 (Lipoproteins, VLDL)
RN  - 0 (Peptide Fragments)
RN  - 0 (Protein Precursors)
RN  - 0 (Triglycerides)
RN  - 0 (very low density lipoprotein triglyceride)
RN  - 11061-68-0 (Insulin)
RN  - 89750-14-1 (glucagon-like peptide 1)
RN  - 9007-92-5 (Glucagon)
SB  - IM
MH  - Blood Glucose/metabolism
MH  - C-Peptide/blood
MH  - Diabetes Mellitus, Non-Insulin-Dependent/*blood/complications/*drug
      therapy
MH  - Female
MH  - Glucagon/*therapeutic use
MH  - Hemoglobin A, Glycosylated/analysis
MH  - Human
MH  - Hyperlipoproteinemia/blood/complications/*drug therapy
MH  - Hypoglycemic Agents/*therapeutic use
MH  - Insulin/blood/therapeutic use
MH  - Lipoproteins, HDL Cholesterol/blood
MH  - Lipoproteins, LDL Cholesterol/blood
MH  - Lipoproteins, VLDL/blood
MH  - Male
MH  - Middle Age
MH  - Peptide Fragments/*therapeutic use
MH  - Protein Precursors/*therapeutic use
MH  - Support, Non-U.S. Gov't
MH  - Time Factors
MH  - Triglycerides/blood
EDAT- 1996/11/01
MHDA- 1996/11/01 00:01
PST - ppublish
SO  - Diabetes Care 1996 Nov;19(11):1200-6.
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UI - 97214432
PMID- 9125510
DA - 19970418
DCOM- 19970418
LR - 20001218
IS - 0021-9150
VI - 121
IP - 2
DP - 1996 Apr 5
TI - High plasma insulin is associated with lower LDL cholesterol in elderly individuals.
PG - 267-73
AB - To investigate possible relationships between plasma low density lipoprotein (LDL) cholesterol and fasting plasma insulin in the elderly, cross-sectional random samples of age cohorts (65, 75, 80 and 85 years, n = 1196, M/F 38/62 percent) were studied in the neighbouring cities of Helsinki and Vantaa, Finland. Plasma total and high density lipoprotein (HDL) cholesterol, plasma triglycerides, blood glucose and plasma insulin were measured after an overnight fast. LDL cholesterol was calculated using the Friedewald equation. Statistical analyses were performed separately in subjects with non-insulin-dependent diabetes mellitus (NIDDM, n = 219) and non-diabetic subjects (n = 969). Comparison of lipid levels by insulin quartile (I < 7.4 IU/l, II 7.4-10.0, III 10.1-15.0, IV > 15.0) showed that total and LDL cholesterol decreased in the highest insulin quartile (P = 0.003). This trend prevailed after adjustments for age, gender, body mass index, blood glucose and serum triglycerides, and it was significant also in normotriglyceridemic (serum triglycerides <2.3 mmol/l) subjects. Furthermore, the association between high insulin and lower cholesterol was seen in normoglycemic (fasting blood glucose <6.7 mmol/l) and diabetic subjects. Lower LDL cholesterol in elderly subjects with higher fasting insulin may reflect poor health or a 'harvesting' effect, but the results may also be due to effects of insulin on LDL catabolism and/or cholesterol absorption.
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AU - Valvanne J
FAU - Salmanen, S
AU - Salmanen S
FAU - Ehnholm, C
AU - Ehnholm C
FAU - Tuomilehto, J
AU - Tuomilehto J
LA - eng
PT - Journal Article
CY - IRELAND
TA - Atherosclerosis
JID - 1242543
RN - 0 (Blood Glucose)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL Cholesterol)
RN - 0 (Triglycerides)
RN - 11061-68-0 (Insulin)
SB - IM
MH - Aged

MH - Aged, 80 and over
MH - Blood Glucose/metabolism
MH - Body Mass Index
MH - Comparative Study
MH - Cross-Sectional Studies
MH - Diabetes Mellitus, Non-Insulin-Dependent/blood
MH - Female
MH - Human
MH - Hyperinsulinemia/*blood
MH - Insulin/*blood
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL Cholesterol/*blood
MH - Male
MH - Random Allocation
MH - Risk Factors
MH - Support, Non-U.S. Gov't
MH - Triglycerides/blood
EDAT- 1996/04/05
MHDA- 1996/04/05 00:01
AID - 0021915095057331 [pii]
PST - ppublish
SO - Atherosclerosis 1996 Apr 5;121(2):267-73.

UI - 96236341
PMID- 8787282
DA - 19960925
DCOM- 19960925
LR - 20001218
IS - 0003-9799
VI - 53
IP - 10-11
DP - 1995
TI - Deterioration of the plasma lipid profile during hospitalization of aged non-insulin-dependent diabetic patients. Comparison with non-diabetic control patients.
PG - 557-60
AB - This study aimed at investigating the changes occurring in the plasma lipid profile of patients with non-insulin-dependent diabetes mellitus (NIDDM) hospitalized for treatment of intercurrent diseases. Twenty-nine non-insulin requiring NIDDM patients (13 men, 16 women; mean age: 67 +/- 2 yrs) and 26 adequately matched patients (12 men, 14 women; mean age: 71 +/- 2 yrs) have been prospectively studied. They were all hospitalized for treatment of various diseases. Diabetic and non-diabetic patients received similar treatment except for intensive insulin therapy in the former group. On admission, diabetic subjects had significantly higher plasma levels of triglycerides and lower levels of HDL cholesterol; during hospitalization, LDL, HDL cholesterol and apo A1 levels increased significantly. In the non-diabetic group, hospitalization and treatment induced significant increases in triglycerides, LDL cholesterol and apo B levels. In conclusion, although insulin treatment during hospitalization of non-insulin requiring NIDDM patients does not fully reverse the abnormal lipid profile, it may help to prevent its further deterioration, particularly by increasing HDL cholesterol levels and hence by decreasing the LDL/HDL cholesterol ratio.
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FAU - Miras, F J
AU - Miras FJ
FAU - de la Higuera, J M

AU - de la Higuera JM
FAU - Castillo, M J
AU - Castillo MJ
LA - eng
PT - Journal Article
CY - FRANCE
TA - Ann Biol Clin (Paris)
JID - 2994690R
RN - 0 (Hypoglycemic Agents)
RN - 0 (Lipids)
RN - 11061-68-0 (Insulin)
SB - IM
MH - Age Factors
MH - Aged
MH - Case-Control Studies
MH - Comparative Study
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/drug therapy
MH - Female
MH - Hospitalization
MH - Human
MH - Hypoglycemic Agents/therapeutic use
MH - Insulin/therapeutic use
MH - Lipids/*blood
MH - Male
MH - Prospective Studies
EDAT- 1995/01/01
MHDA- 1995/01/01 00:01
PST - ppublish
SO - Ann Biol Clin (Paris) 1995;53(10-11):557-60.

UI - 93215417
PMID- 8462384
DA - 19930506
DCOM- 19930506
LR - 20001219
IS - 0149-5992
VI - 16
IP - 4
DP - 1993 Apr
TI - Effects of gemfibrozil on low-density lipoprotein particle size, density distribution, and composition in patients with type II diabetes.
PG - 584-92
AB - OBJECTIVE--To study the effects of gemfibrozil treatment on LDL particle size, density distribution, and composition in NIDDM patients. RESEARCH DESIGN AND METHODS--We performed LDL analyses on 16 NIDDM patients with stable glycemic control. They were randomly allocated to receive either gemfibrozil (n = 8) or a placebo (n = 8) for 3 mo in a double-blind study. The LDL particle size distribution and the particle diameter of the major LDL peak were measured with nondenaturing polyacrylamide gradient gel electrophoresis. The density distribution and composition of LDL were determined with the density gradient ultracentrifugation method. RESULTS--In the gemfibrozil group the mean serum TG concentration decreased by 38%, HDL cholesterol concentration increased by 10%, and LDL cholesterol concentration by 17% (P < 0.05). During gemfibrozil therapy the mean particle diameter of the major LDL peak increased from 244 to 251 A (P < 0.05), whereas in the placebo group the mean LDL particle diameter remained unchanged. We found an inverse correlation between the changes of serum TG and the particle diameters of the major LDL peak (r = 0.85, P < 0.01). Gemfibrozil produced a shift in the LDL density distribution toward lower density. The mean peak density decreased from 1.0371 to 1.0345 g/ml because of a significant rise in the light LDL concentration from 141.0 to 193.2 mg/dl (P < 0.05), whereas the concentration of dense LDL had a

tendency to decrease. In the placebo group the LDL density distribution did not change. Gemfibrozil increased the CE-to-TG ratio in LDL core lipids by 27% (P < .05), otherwise, the LDL composition was only slightly affected. CONCLUSIONS--The results indicate gemfibrozil-induced changes in LDL properties in NIDDM patients are similar to those previously reported in nondiabetic individuals and are related to changes in serum TG level.

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FAU - Kuusi, T
AU - Kuusi T
FAU - Taskinen, M R
AU - Taskinen MR
LA - eng
PT - Clinical Trial
PT - Journal Article
PT - Randomized Controlled Trial
CY - UNITED STATES
TA - Diabetes Care
JID - 7805975
RN - 0 (Apolipoproteins B)
RN - 0 (Blood Glucose)
RN - 0 (C-Peptide)
RN - 0 (Hemoglobin A, Glycosylated)
RN - 0 (Hypoglycemic Agents)
RN - 0 (Lipoproteins, HDL Cholesterol)
RN - 0 (Lipoproteins, LDL)
RN - 0 (Lipoproteins, VLDL)
RN - 0 (Phospholipids)
RN - 0 (Placebos)
RN - 0 (Triglycerides)
RN - 25812-30-0 (Gemfibrozil)
RN - 657-24-9 (Metformin)
SB - IM
MH - Apolipoproteins B/blood
MH - Blood Glucose/metabolism
MH - C-Peptide/blood
MH - Diabetes Mellitus, Non-Insulin-Dependent/*blood/*drug therapy
MH - Double-Blind Method
MH - Female
MH - Gemfibrozil/*therapeutic use
MH - Hemoglobin A, Glycosylated/analysis
MH - Human
MH - Hypoglycemic Agents/*therapeutic use
MH - Lipoproteins, HDL Cholesterol/blood
MH - Lipoproteins, LDL/*blood
MH - Lipoproteins, VLDL/blood
MH - Male
MH - Metformin/therapeutic use
MH - Middle Age
MH - Phospholipids/blood
MH - Placebos
MH - Support, Non-U.S. Gov't
MH - Triglycerides/blood
EDAT- 1993/04/01
MHDA- 1993/04/01 00:01
PST - ppublish
SO - Diabetes Care 1993 Apr;16(4):584-92.

1: Atherosclerosis 2001 May;156(1):209-16

Effect of intensive lipid-lowering strategy on low-density lipoprotein particle size in patients with type 2 diabetes mellitus.

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A preponderance of small dense LDL particles is strongly associated with the occurrence of atherosclerotic disease. Although several studies have documented an increased prevalence of small dense LDL particles in diabetes mellitus no data are available to show the effect of lipid-lowering treatment upon the improvement of LDL particle size. In the present study we examined the effect of lipid-lowering treatment, following an intensive lipid-lowering strategy for 30 weeks pursuing ADA recommended target lipid levels, on LDL particle size in 50 type 2 diabetic patients with moderate hyperlipidemia. At week 0, 24 patients (48%) were characterized by small dense LDL phenotype pattern B. After the treatment period a shift towards normal LDL particle size was observed in 17 patients but seven patients (28%) showed the more atherogenic LDL subclass pattern B. After treatment, plasma HDL-cholesterol was significantly lower ($P<0.05$) in these patients compared to those who had LDL subclass pattern A. Multivariate regression analysis revealed VLDL-cholesterol or triglycerides and HDL(3)-cholesterol as independent determinants for LDL particle size. Change in HDL(2)-cholesterol was an independent determinant for change in LDL particle size. In conclusion, a strategy of intensive lipid-lowering, with the intention to reduce triglyceride levels below 1.7 mmol/l, may be insufficient to ensure improvement in LDL size in all patients.

PMID: 11369016 [PubMed - indexed for MEDLINE]

2: J Clin Endocrinol Metab 2000 Nov;85(11):4188-92

Effect of insulin and sulfonylurea therapy, at the same level of blood glucose control, on low density lipoprotein subfractions in type 2 diabetic patients.

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The aim of this study was to evaluate the effect of sc insulin (INS) compared with sulfonylurea (SUL) therapy, at the same level of blood glucose control, on the low density lipoprotein (LDL) subfraction profile in normolipidemic type 2 diabetic patients. Nine normolipidemic type 2 diabetic men (age, 56+/-3 yr; body mass index, 26.5+/-0.8 kg/m2, mean +/- SEM), after a 3-week wash-out period, were assigned to INS or SUL for 2 months in a randomized cross-over design. Doses were adjusted only during the first month and then were kept constant. At the end of the treatments, hemoglobin A1c, plasma lipids, LDL, and very low density lipoprotein (VLDL) subfraction profiles and plasma postheparin lipoprotein lipase and hepatic lipase (HL) activities were evaluated. Despite glucose control was similar at the end of both periods (hemoglobin A1c, 7.4+/-0.3% vs. 7.0+/-0.2%, INS vs. SUL), INS compared with SUL significantly reduced plasma triglyceride (1.9+/-0.1 vs. 2.1+/-0.1 mmol/L; $P < 0.05$). Although INS did not affect the LDL concentration, it induced a decrease in both the amount (% Δ = 9.6 vs. 76.1+/-16.8 mg/dL; P = NS) and the proportion (31.2+/-3.0% vs. 36.3+/-3.5%, $P < 0.05$) of small LDL. Moreover, the decrease in small LDL was positively related to the reduction of large VLDL ($r = 0.67$; $P < 0.04$) and HL ($r = 0.69$, $P < 0.05$) induced by insulin therapy. In conclusion, sc insulin therapy, independently of glucose control and even in the presence of

quite low plasma triglyceride levels, is able to reduce small LDL particles in type 2 diabetic patients. This change is related to decreases in both HL activity and large VLDL particles.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 11095452 [PubMed - indexed for MEDLINE]

3: Nutr Metab Cardiovasc Dis 2000 Aug;10(4):204-8

Lipid and lipoprotein patterns in type 2 non-obese diabetic patients. Do Lp(a) levels decrease with improved glycemic control in these patients?

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BACKGROUND AND AIM: In this study, we investigated the levels of apolipoprotein-AI (apo-AI), apolipoprotein (apo-B), triglyceride (TG), high-density-lipoprotein-cholesterol (HDL-C), low-density-lipoprotein-cholesterol (LDL-C), total cholesterol, lipoprotein(a) in a group of non-obese, type 2 diabetes mellitus patients with different types of treatment and a control group of non-obese, non-diabetic subjects. METHODS AND RESULTS: Patients were divided into three groups according to their treatment types: insulin, sulphonylurea and untreated groups. All groups were similar in sex, weights, known duration of diabetes and habits. Each group consisted of 30 subjects. There were no differences in apo-AI, apo-B and TG levels ($p > 0.05$), whereas HDL-C levels in the untreated group were significantly lower than those of the other groups ($p < 0.05$). Lp(a) levels in the untreated group were higher than in the other ($p < 0.05$). CONCLUSIONS: Gaining metabolic control in diabetes mellitus is crucial in pulling back lipid, lipoprotein and apolipoprotein levels to a desired level and in attenuating CAD (coronary artery disease) risk factors, and also in preventing CAD. Lp(a) levels in particular are decreased by insulin or sulfonylurea in non-obese patients with type 2 diabetes mellitus.

PMID: 11079288 [PubMed - indexed for MEDLINE]

4: Diabetes Metab Res Rev 2000 Mar-Apr;16(2):82-7

Pravastatin compared to bezafibrate in the treatment of dyslipidemia in insulin-treated patients with type 2 diabetes mellitus.

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BACKGROUND: Both HMG-CoA reductase inhibitors and fibric acid derivates are used for the treatment of dyslipidemia in Type 2 diabetes patients. The aim of this study was to compare the lipid lowering effect of 40 mg pravastatin, a HMG-CoA reductase inhibitor, and 400 mg bezafibrate, a fibric acid derivate, on serum lipids, lipoproteins and lipoprotein composition in 45 (22 men and 23 women) dyslipidemic, insulin-treated Type 2 diabetes patients. METHOD: The study used a double-blind, cross-over design. RESULTS: Pravastatin treatment was more effective in reducing total cholesterol, LDL-cholesterol, LDL-triglycerides, LDL-ApoB and LDL/HDL-cholesterol ratio (all $p<0.001$ between groups) and total/HDL-cholesterol and ApoAI/LDL-ApoB ratios (both $p<0.01$) and always induced a decrease in LDL-cholesterol concentrations and LDL/HDL-cholesterol ratio

irrespective of baseline triglyceride concentration. Bezafibrate was more effective in increasing HDL-cholesterol (p<0.01 between groups), ApoAI lipoprotein and decreasing triglycerides (both p<0.001 between groups) but induced an increase in LDL-cholesterol concentration particularly in patients with baseline triglyceride concentrations exceeding 2.0 mmol/l. With bezafibrate treatment the LDL-cholesterol/LDL-ApoB ratio showed a tendency to rise, suggesting a change in the LDL particle composition to a less small and dense form, while pravastatin treatment induced a decrease in this ratio suggesting a change in the LDL particle to a more dense form. With pravastatin treatment a small rise in HbA(1c) was observed. CONCLUSION: Pravastatin treatment is superior in lowering cholesterol-enriched lipoprotein subpopulations and improving cardiovascular risk factors. Bezafibrate is more effective in raising HDL-cholesterol and alters LDL particle composition to a more favorable form.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 10751747 [PubMed - indexed for MEDLINE]

5: West Afr J Med 2000 Jan-Mar;19(1):27-33

The effect of glycaemic control on the prevalence and pattern of dyslipidaemia in Nigerian patients with newly diagnosed non insulin dependent diabetes mellitus.

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Dyslipidaemia (DL) is a common condition in patients with NIDDM, but its prevalence and the effect of glycaemic control on the disorder have only been scantily reported in Nigerians. The present study is therefore aimed at determining the effect of diabetic control on prevalence and pattern of DL in Nigerian patients with NIDDM. Thirty six diabetics were followed up for 24 weeks. Indices determined included anthropometric measurements, fasting (FBG) and two hour post prandial blood glucose (2 hours PPBG), together with glycated haemoglobin (GHb) levels, and fasting lipids at presentation, 12 and after 24 weeks of treatment. The prevalence rates of raised total cholesterol/high density lipoprotein cholesterol (TC/HDL) ratio reduced HDL-cholesterol and mixed DL decreased significantly between 0-week and 24 weeks of treatment (57.1% vs 14.3% 50% vs 11.4% and 44% vs 22.2% respectively, P < 0.001 for each). The proportion of patient with elevated low-density lipoprotein-cholesterol also decreased significantly from 21.4% at 0-week to 8.8 after 24 weeks (P < 0.025). On the other hand, the prevalence of hypercholesterolaemia and hypertriglyceridaemia were not significantly changed between 0 and 24 weeks (P > 0.05). Patients with DL despite treatment were characterised by higher FBG at 24 weeks of treatment compared with normolipidaemic patients (P < 0.001). It is concluded from this study that improved glycaemic control reduced some dyslipidaemia, and may therefore suffice to correct them in some Nigerian patients with NIDDM.

PMID: 10821083 [PubMed - indexed for MEDLINE]

6: Diabet Med 1999 Oct;16(10):821-6

The lipoprotein profile differs during insulin treatment alone and combination therapy with insulin and sulphonylureas in patients with Type 2 diabetes mellitus.

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AIMS: To study whether changes in endogenous insulin secretion at the same glycaemic control affect the plasma concentrations of lipoproteins in patients with Type 2 diabetes mellitus. METHODS: Fifteen patients, age 59+/-2 years (mean +/- SEM), body weight 96.3+/-3.0kg, body mass index 29.6+/-0.9 kg/m2 were treated with sulphonylurea and insulin in combination or with insulin alone in a randomized, double-blind, crossover study. All patients were treated with a multiple daily injection regimen with the addition of glibenclamide 10.5 mg daily or placebo tablets. RESULTS: During combination therapy, the dose of insulin was 25% less (P < 0.002) and there was a 29% increase in plasma C-peptide concentration (P = 0.01). Plasma levels of free insulin were not changed. Plasma levels of sex hormone-binding globulin (SHBG) and insulin-like growth factor-binding protein (IGFBP)-1 were lowered. There were no differences in the 24-h blood glucose profiles or HbA1c (6.0+/-0.2 vs. 6.3+/-0.2%; P = 0.16). Body weight was similar. There was a significant decrease in plasma LDL cholesterol (3.04+/-0.24 vs. 3.41+/-0.21 mmol/l; P = 0.04), apolipoprotein A1 and of lipoprotein(a) but an increase in VLDL-triglycerides (1.36+/-0.31 vs. 0.96+/-0.16 mmol/l; P = 0.02) during combination therapy. The ratio between LDL cholesterol and apolipoprotein B concentrations was significantly lower during combination therapy (P < 0.01). CONCLUSIONS: Combination therapy with insulin and sulphonylureas increases portal insulin supply and thereby alters liver lipoprotein metabolism when compared with insulin therapy alone.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 10547208 [PubMed - indexed for MEDLINE]

7: Acta Cardiol 1999 Aug;54(4):203-7

Plasma lipoprotein (a) levels in Turkish NIDDM patients with and without vascular diabetic complications.

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OBJECTIVE: Plasma concentrations of lipoprotein (a) [Lp(a)], an independent risk factor for atherosclerosis, were measured in 59 non-insulin-dependent diabetes mellitus (NIDDM) patients with and without vascular complications, and 21 non-diabetic healthy subjects. RESULTS: The plasma log Lp(a) levels were found to be significantly increased in the NIDDM patients (1.40 +/- 0.36) compared with the healthy subjects (1.02 +/- 0.53; p < 0.05). Plasma Lp(a) levels in NIDDM patients with diabetic vascular complications (1.51 +/- 0.27) were significantly higher than those of the NIDDM patients without diabetic vascular complications (1.23 +/- 0.43) and healthy subjects (p < 0.05). There were significant correlations between plasma log Lp(a) levels and apolipoprotein B (apo B) in all NIDDM patients (r: 0.68, p < 0.05). No correlation was observed between Lp(a) levels and age, sex, duration of diabetes, fasting blood glucose, haemoglobin A1c, the mode of treatment, triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and apolipoprotein A1 levels in all patients. CONCLUSIONS: It was concluded that Lp(a) was a risk factor for angiopathy in NIDDM patients and the patients who have a high plasma Lp(a) concentration should be kept under strict glycaemic control.

PMID: 10511996 [PubMed - indexed for MEDLINE]

8: Acta Diabetol. 1999 Jun;36(1-2):27-33

The effect of gemfibrozil on lipid profile and glucose metabolism in hypertriglyceridaemic well-controlled non-insulin-dependent diabetic patients. For the Gemfibrozil Study Group.

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We assessed the efficacy of gemfibrozil therapy on lipid profile and glucose metabolism in a large cohort of (type 2) non-insulin-dependent diabetic patients. We enrolled 217 type 2 diabetic patients with plasma triglyceride concentrations equal to or above 2 mmol/l: 110 were randomized to gemfibrozil (600 mg twice daily) and 107 to placebo treatment in a double blind fashion. Each treatment was followed for 20 weeks. To assess postprandial glucose metabolism and insulin secretion, at time 0 and 20 weeks, a standard meal containing 12.5 g of proteins, 40.1 g of carbohydrate, 10 g of lipids was given. No differences in demographic characteristics were observed between patients randomized either to gemfibrozil or to placebo therapy. No differences were observed in total cholesterol and LDL-cholesterol concentration changes between the baseline observations and week 20 of both treatments. At variance, both treatments significantly increased HDL cholesterol. Gemfibrozil treatment significantly decreased plasma triglyceride concentration from 316+/-34 to 214+/-82 mg/dl ($P < 0.001$), whereas with placebo triglyceride levels increased from 318 + 93 to 350 + 217 mg/dl. No changes were observed in non-esterified fatty acid concentrations or in fasting plasma glucose concentrations, in HbA(1C) values, insulin and C-peptide concentrations. Gemfibrozil treatment: 1) significantly reduces circulating triglyceride concentration; 2) does not significantly affect cholesterol concentration; 3) does not worsen glucose metabolism.

Publication Types:
Clinical Trial
Multicenter Study
Randomized Controlled Trial

PMID: 10436249 [PubMed - indexed for MEDLINE]

9: Metabolism. 1999 Feb;48(2):252-8

Long-lasting antidiabetic effect of a dipeptidyl peptidase IV-resistant analog of glucagon-like peptide-1.

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Glucagon-like peptide-1(7-37) (GLP-1) is the most potent insulinotropic hormone characterized thus far. Because its activity is preserved in non-insulin-dependent diabetes mellitus (NIDDM) patients, it is considered a potential new drug for the treatment of this disease. One limitation in its therapeutic use is a short half-life in vivo (5 minutes), due in part to a fast degradation by the endoprotease dipeptidylpeptidase IV (DPPIV). Recently, it was reported that GLP-1 became resistant to DPPIV when the alanine residue at position 8 was replaced by a glycine (GLP-1-Gly8). We report here that this change slightly decreased the affinity of the peptide for its receptor (IC50, 0.41 +/- 0.14 and 1.39 +/- 0.61 nmol/L for GLP-1 and GLP-1-Gly8, respectively) but did not change the efficiency to stimulate accumulation of intracellular cyclic adenosine monophosphate (cAMP) (EC50, 0.25 +/- 0.05 and 0.36 +/- 0.06 nmol/L for GLP-1 and GLP-1-Gly8, respectively). Second, we demonstrate for the

first time that this mutant has an improved insulinotropic activity compared with the wild-type peptide when tested in vivo in an animal model of diabetes. A single injection of 0.1 nmol GLP-1-Gly8 in diabetic mice fed a high-fat diet can correct fasting hyperglycemia and glucose intolerance for several hours, whereas the activity of 1 nmol GLP-1 vanishes a few minutes after injection. These actions were correlated with increased insulin and decreased glucagon levels. Interestingly, normoglycemia was maintained over a period that was longer than the predicted peptide half-life, suggesting a yet undescribed long-term effect of GLP-1-Gly8. GLP-1-Gly8 thus has a markedly improved therapeutic potential compared with GLP-1, since it can be used at much lower doses and with a more flexible schedule of administration.

PMID: 10024091 [PubMed - indexed for MEDLINE]

10: Ann N Y Acad Sci 1999 Dec 11;865:336-43

On the treatment of diabetes mellitus with glucagon-like peptide-1.

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As a therapeutic principle, the insulinotropic peptide, GLP-1, of the secretin-glucagon family of peptides, has turned out to possess some remarkably attractive properties, including the capability of normalizing blood glucose concentrations in patients with non-insulin-dependent diabetes mellitus and promoting satiety and reducing food intake in healthy volunteers. Because of rapid and extensive metabolization, the peptide is not immediately clinically applicable and, as a therapeutic principle, GLP-1 is still in its infancy. Some possible avenues for circumventing these difficulties are the development of DPP-IV-resistant analogs, the inhibition of DPP-IV, enhancement of GLP-1 secretion, GLP delivery systems using continuous subcutaneous infusion or buccal tablets, GLP-1 absorption, and orally active, stable analogs. It seems likely that one or more of these approaches could result in a clinically useful development program.

Publication Types:
Review
Review, Tutorial

PMID: 9928027 [PubMed - indexed for MEDLINE]

11: Diabetes Care 1999 May;21(5):701-5

Comment in:
Diabetes Care. 1999 Mar;22(3):528.

The effects of metformin on glycemic control and serum lipids in insulin-treated NIDDM patients with suboptimal metabolic control.

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OBJECTIVE: To test the hypothesis that metformin therapy, given as an adjunct to insulin therapy, improves metabolic control in insulin-treated NIDDM patients with suboptimal glycemic control. RESEARCH DESIGN AND METHODS: A total of 33 subjects with insulin-treated NIDDM were investigated; all had commenced insulin after secondary failure of antihyperglycemic agents. Two randomized double-blind

placebo-controlled crossover studies were run. In study 1 (n = 19), insulin-treated subjects with suboptimal glycemic control received 12 weeks of metformin 1 g b.i.d. and 12 weeks of placebo. In study 2 (n = 14), subjects already established on adjunctive metformin-insulin therapy stopped the metformin component and received 12 weeks of metformin at their baseline dosage (range 1-2.5 g) and 12 weeks of equivalent placebo. Fasting plasma glucose, HbA1c, and serum lipids were measured at baseline and midway through and at the end of each treatment phase. The effect of 12 weeks of metformin treatment was compared with the effect of 12 weeks of placebo in each study and in both studies combined. RESULTS: In study 1, metformin treatment was associated with significant improvements in fasting plasma glucose (mean 12-week difference from placebo [95% CI]: 5.5 mmol/l [3.6-7.1], P < 0.001) and HbA1c (1.6% [0.9-2.4], P < 0.001). In study 2, metformin treatment was associated with significantly lower fasting plasma glucose (5.3 mmol/l [0.6-9.9], P = 0.029) and lower HbA1c (2.4% [1.0-3.8], P = 0.003) compared with those for placebo. Study 2 also showed metformin treatment to be associated with significantly lower total cholesterol than that for placebo (1.0 mmol/l [0.1-1.9], P = 0.032) and lower LDL cholesterol (1.0 mmol/l [0.1-1.9], P = 0.028). This significant difference in serum lipids seen in study 2 was not seen in study 1, but was present when both sets of data were combined (n = 33, mean total cholesterol difference at 12 weeks [95% CI]: 0.6 mmol/l [0.1-1.1], P = 0.015). Metformin had no significant effect on triglyceride, HDL cholesterol, weight, or blood pressure. Two subjects on metformin withdrew because of side effects. CONCLUSIONS: Metformin, when given as adjunctive therapy, was well tolerated and improved glycemic control and lipid concentrations in patients with insulin-treated NIDDM whose diabetes was poorly controlled. These improvements could be maintained over the long term.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 9540227 [PubMed - indexed for MEDLINE]

12: Diabetes Care 1998 Apr;21(4):477-81

Treatment of hypercholesterolemia and combined hyperlipidemia with simvastatin and gemfibrozil in patients with NIDDM. A multicenter comparison study.

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OBJECTIVE: To compare the lipid-lowering efficacies of simvastatin and gemfibrozil in NIDDM patients with combined (mixed) hyperlipidemia (CHL) or isolated hypercholesterolemia (IHC). RESEARCH DESIGN AND METHODS: Patients with primary dyslipidemia and NIDDM were recruited for this double-blind, double-dummy comparison study from 10 Finnish centers. After a 4-week placebo run-in period, they were randomly assigned to simvastatin or gemfibrozil. The simvastatin group (n = 47) received 10 mg once nightly for 6 weeks, 20 mg for the next 6 weeks, and 40 mg for the third 6-week period. The gemfibrozil group (n = 49) received 600 mg twice daily throughout the 24 weeks. The lipid-lowering efficacies of both drugs were compared in all patients as well as separately in patients with CHL and IHC. RESULTS: In all patients, simvastatin reduced LDL and total cholesterol and the LDL-to-HDL cholesterol ratio more effectively, whereas gemfibrozil was more effective in elevating HDL cholesterol and decreasing triglyceride levels. The drug effects differed according to lipid phenotype at baseline. Simvastatin decreased LDL cholesterol levels by 30-40% in both phenotypes. Gemfibrozil caused a 15% reduction in LDL cholesterol in IHC but no change in CHL patients. Simvastatin produced 16-30% reductions in triglyceride levels in CHL but no change in IHC patients. Gemfibrozil caused reductions in triglycerides in CHL "50% and more" and in IHC "40%" patients, with 12-18% increases in HDL cholesterol in these groups. CONCLUSIONS: Simvastatin is useful

in both CHL and IHC patients, whereas gemfibrozil can be used in patients with high triglyceride and low or normal LDL cholesterol levels

Publication Types:
Clinical Trial
Multicenter Study
Randomized Controlled Trial

PMID: 9571327 [PubMed - indexed for MEDLINE]

13: J Clin Invest 1998 Apr 1;101(7):1421-30

Exendin(9-39)amide is an antagonist of glucagon-like peptide-1(7-36)amide in humans.

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The gastrointestinal hormone, glucagon-like peptide-1(7-36)amide (GLP-1) is released after a meal. The potency of synthetic GLP-1 in stimulating insulin secretion and in inhibiting glucagon secretion indicates the putative physiological function of GLP-1. In vitro, the non-mammalian peptide, exendin(9-39)amide [ex(9-39)NH2], is a specific and competitive antagonist of GLP-1. This in vivo study examined the efficacy of ex(9-39)NH2 as an antagonist of exogenous GLP-1 and the physiological role of endogenous GLP-1. Six healthy volunteers underwent 10 experiments in random order. In each experiment, a 30-min period of euglycemia was followed by an intravenous infusion of glucose for 150 min that established a stable hyperglycemia of 8 mmol/liter. There was a concomitant intravenous infusion of one of the following: (1) saline, (2) GLP-1 (for 60 min at 0.3 pmol . kg-1 . min-1 that established physiological postprandial plasma levels, and for another 60 min at 0.9 pmol . kg-1 . min-1 to induce supraphysiological plasma levels), (3-5) ex(9-39)NH2 at 30, 60, or 300 pmol . kg-1 . min-1 + GLP-1, (6-8) ex(9-39)NH2 at 30, 60, or 300 pmol . kg-1 . min-1 + saline, (9 and 10) GIP (glucose-dependent insulinotropic peptide; for 60 min at 0.8 pmol . kg-1 . min-1, with saline or ex(9-39)NH2 at 300 pmol . kg-1 . min-1). Each volunteer received each of these concomitant infusions on separate days. ex(9-39)NH2 dose-dependently reduced the insulinotropic action of GLP-1 with the inhibitory effect declining with increasing doses of GLP-1. ex(9-39)NH2 at 300 pmol . kg-1 . min-1 blocked the insulinotropic effect of physiological doses of GLP-1 and completely antagonized the glucagonostatic effect at both doses of GLP-1. Given alone, this load of ex(9-39)NH2 increased plasma glucagon levels during euglycemia and hyperglycemia. It had no effect on plasma levels of insulin during euglycemia but decreased plasma insulin during hyperglycemia. ex(9-39)NH2 did not alter GIP-stimulated insulin secretion. These data indicate that in humans, ex(9-39)NH2 is a potent GLP-1 antagonist without any agonistic properties. The pancreatic A cell is under a tonic inhibitory control of GLP-1. At hyperglycemia, the B cell is under a tonic stimulatory control of GLP-1.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 9525989 [PubMed - indexed for MEDLINE]

14: Isr J Med Sci 1997 Oct;33(10):690-5

Glucagon-like peptide-1 structure, function and potential use for NIDDM.

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Basic research on the cellular mechanisms that control the expression of the gene encoding glucagon has led to the discovery of proglucagon. This precursor is processed by tissue-specific proteolysis to produce glucagon in pancreatic alpha-cells and a glucagon-like peptide-1 (GLP-1) in the intestine. GLP-1 is a hormone that is released by intestinal cells into the circulation in response to food intake. GLP-1 and gastric inhibitory peptide (GIP) which has also been termed glucose-dependent insulinotropic peptide appear to account for most of the incretin effect in the augmentation of glucose-stimulated insulin secretion. These two hormones have specific beta-cell receptors that are coupled to GTP binding proteins to induce production of cyclic AMP and activation of cyclic AMP-dependent protein kinase. It is proposed that at least one factor contributing to the pathogenesis of non-insulin-dependent diabetes mellitus (NIDDM) is desensitization of the GLP-1 receptor on beta-cells. At pharmacological doses, infusion of GLP-1, but not of GLP, can improve and enhance postprandial insulin response in NIDDM patients. Agonists of GLP-1 receptor have been proposed as new potential therapeutic agents in NIDDM patients. The observations that GLP-1 induces both secretion and production of insulin, and that its activities are mainly glucose-dependent, led to the suggestion that GLP-1 may present a unique advantage over sulfonylurea drugs in the treatment of NIDDM.

Publication Types:
Review
Review, Tutorial

PMID: 9297146 [PubMed - indexed for MEDLINE]

15: Diabetes Care 1997 Sep;20(9):1459-61

Lack of change of lipoprotein(a) levels by the optimization of glycemic control with insulin therapy in NIDDM patients.

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OBJECTIVE: To evaluate the effect of glycemic control improvement with insulin therapy on lipoprotein(a) [Lp(a)] levels in patients with NIDDM. RESEARCH DESIGN AND METHODS: We performed a longitudinal study in a tertiary referral center to compare lipid and Lp(a) levels before and after 3 months of insulin therapy in 60 poorly controlled NIDDM patients (32 men, 28 women). Patients previously treated with oral hypoglycemic agents (n = 50) received one to two insulin doses, and those previously treated with insulin (n = 10) received multiple insulin doses. Lp(a) levels were measured by the Terumo method. Differences between the two periods were assessed by the paired t test and Wilcoxon's test. RESULTS: After 3 months of insulin therapy, HbA1c decreased from 9.6 +/- 1.9 to 6.2 +/- 1.4% (P < 0.0005) in all patients and from 9.1 +/- 2.1 to 6.1 +/- 2.9% (P < 0.05) in patients under multiple insulin doses, being < or = 6.0% in 59% of patients. Total triglyceride and VLDL cholesterol levels decreased (P < 0.01) and HDL cholesterol increased significantly (P < 0.0005). However, no changes in Lp(a) levels were observed in all patients (25.3 +/- 25.0 vs 25.7 +/- 27.2% mg/dl) and in patients with baseline Lp(a) levels above (63.5 +/- 15.5 vs. 65.1 +/- 23.1 mg/dl) or below 30 mg/dl (11.5 +/- 5.5 vs. 11.5 +/- 7.3 mg/dl). In addition, patients reaching HbA1c levels < or = 6.0% or > 6.0% presented similar Lp(a) levels (26.3 +/- 29.1 vs 25.3 +/- 25.0 mg/dl). Moreover, no correlations were observed between changes in Lp(a) levels and in the glycemic control parameters. CONCLUSIONS: This study shows that the improvement of glycemic

control by insulin therapy does not influence plasma Lp(a) levels, measured by the Terumo method, in NIDDM patients, independently of baseline values and the degree of glycemic control reached.

PMID: 9283797 [PubMed - indexed for MEDLINE]

16: Diabetes 1997 Jul;46(7):1207-13

Optimization of glycemic control by insulin therapy decreases the proportion of small dense LDL particles in diabetic patients.

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Small dense LDL particles (B phenotype) are considered to be more atherogenic than large buoyant LDL particles. The influence of glycemic control on LDL particle size and density is still under debate. The aim of this study was to determine LDL subfraction phenotype in both IDDM and NIDDM patients in poor glycemic control compared with that of respective matched control groups. In addition, we evaluated the effect of a 3-month period of optimized glycemic control on this parameter. Thirty-seven IDDM patients and 33 NIDDM patients, together with two respective age-, sex-, and BMI-matched control groups were studied. Non-A phenotype prevalence in IDDM patients before (19%) and after blood glucose optimization (11%) was similar to that of their control group (12%). However, NIDDM patients displayed a higher proportion of the non-A phenotype (51%) than did the control group (28%), but it became closer (30%, P < 0.05) after glycemic control improved. All subjects with non-A phenotype that changed to A phenotype showed triglyceride levels below 1.63 mmol/l and a greater decrease in HbA1c than did subjects whose phenotype did not change (4.9 +/- 1.5 vs. 3.1 +/- 1.4%, P < 0.05). A higher proportion of small dense LDL was observed in NIDDM women than in nondiabetic women (LDL5 10.0 +/- 4.8 vs. 6.3 +/- 1.5%, LDL6 6.1 +/- 2.2 vs. 4.2 +/- 0.8%, P < 0.05) during both stages of glycemic control, but no differences were observed between NIDDM and nondiabetic men. In conclusion, these findings provide new evidence for the relevance of near-normal glycemic control in the prevention of macrovascular disease and could contribute to an explanation of the loss of protection for cardiovascular disease in diabetic women.

PMID: 9200657 [PubMed - indexed for MEDLINE]

17: Diabetologia 1997 Jul;40(7):843-9

Short-term oestrogen replacement therapy improves insulin resistance, lipids and fibrinolysis in postmenopausal women with NIDDM.

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Oestrogen replacement therapy is associated with a decreased risk of cardiovascular disease in postmenopausal women. Patients with non-insulin-dependent diabetes mellitus (NIDDM) have an increased cardiovascular risk. However, oestrogen replacement therapy is only reluctantly prescribed for patients with NIDDM. In a double blind randomized placebo controlled trial we assessed the effect of oral 17 beta-estradiol during 6 weeks in 40 postmenopausal women with NIDDM. Glycated haemoglobin (HbA1c), insulin sensitivity, suppressibility of hepatic glucose production, lipoprotein profile and parameters of fibrinolysis were determined. The oestrogen treated group

demonstrated a significant decrease of HbA1c and in the normotriglyceridaemic group a significantly increased suppression of hepatic glucose production by insulin. Whole body glucose uptake and concentrations of non-esterified fatty acids did not change. LDL-cholesterol- and apolipoprotein B levels decreased, and HDL-cholesterol, its subfraction HDL2-cholesterol and apolipoprotein A1 increased. The plasma triglyceride level remained similar in both groups. Both the concentration of plasminogen activator inhibitor-1 antigen and its active subfraction decreased. Tissue type plasminogen activator activity increased significantly only in the normotriglyceridaemic group. Oestrogen replacement therapy improves insulin sensitivity in liver, glycaemic control, lipoprotein profile and fibrinolysis in postmenopausal women with NIDDM. For a definite answer as to whether oestrogens can be more liberally used in NIDDM patients, long term studies including the effect of progestogens are necessary.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 9243107 [PubMed - indexed for MEDLINE]

18: Atherosclerosis 1997 Jan 3;128(1):113-9

Plasma lipoproteins and incidence of non-insulin-dependent diabetes mellitus in Pima Indians: protective effect of HDL cholesterol in women.

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The role of plasma lipoproteins in the development of non-insulin-dependent diabetes mellitus (NIDDM) was studied in 787 non-diabetic (2-h glucose < 11.1 mmol/l) Pima Indians (265 men and 522 women). Subjects were followed for a mean of 9.8 (range: 1.8-16.4) years, during which 261 (76 men and 185 women) developed NIDDM. In men and women, very-low-density lipoprotein (VLDL) cholesterol, VLDL triglyceride, low-density lipoprotein triglyceride and total triglyceride, controlled for age, predicted NIDDM (P < 0.01 for each). These effects diminished when controlled for age, sex, body mass index, systolic blood pressure and 2-h glucose. However, high-density lipoprotein (HDL) cholesterol, controlled for age, body mass index, systolic blood pressure and 2-h glucose, was a significant protective factor for NIDDM in women (hazard rate ratio (HRR) = 0.35, 95% CI (0.23-0.54), P < 0.001, 90th compared with 10th percentile) but not in men (HRR = 1.04, 95% CI (0.53-2.05), P = 0.915). This association remained significant in women when controlled for fasting or 2-h plasma insulin concentrations, other estimates of insulin resistance or alcohol consumption. The protective effect of HDL cholesterol was similar among women with normal (2-h glucose < 7.8 mmol/l) or impaired (7.8 mmol/l < or = 2-h glucose < 11.1 mmol/l) glucose tolerance at baseline. These results indicate that lipoprotein disorders are an early accompaniment of the abnormalities that lead to NIDDM.

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19: Acta Biol Hung 1997;48(3):355-67

Treatment possibility of hypercholesterolaemia associated with hypertriglyceridaemia.

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Thirty patients were investigated with hyperlipoproteinaemia, 15 patients with non-insulin dependent diabetes mellitus (NIDDM) and 15 with primary hyperlipoproteinaemia. The patients took 250 mg acipimox (5-metyl-pyrazine-carboxylic acid 4-oxide) 3 times per day for 2 months. Serum examinations were performed before and after 1 and 2 months of acipimox administration. After treatment the cholesterol and triglyceride levels decreased in both groups. Patients with NIDDM had 11% increase of high density lipoprotein-cholesterol (HDL-C) level at the end of the first, and 19% increase at the end of the second month, while patients with primary hyperlipoproteinaemia did not change significantly. The low density lipoprotein (LDL) level did not change significantly in either groups of patients. The apolipoprotein A 1 (apo A 1) levels increased significantly during the second month of acipimox administration. Uric acid levels decreased in both groups, but significant change could be detected mainly in the NIDDM group. Serum glucose level did not change in the non-diabetic patients, while it decreased significantly in the NIDDM group.

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20: Diabetes Care 1996 Nov;19(11):1200-6

The antidiabetogenic effect of GLP-1 is maintained during a 7-day treatment period and improves diabetic dyslipoproteinemia in NIDDM patients.

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OBJECTIVE: To investigate the long-term antidiabetogenic effect of glucagon-like peptide 1 (GLP-1) and its influence on diabetic dyslipoproteinemia, patients with NIDDM were treated with GLP-1 subcutaneously for 1 week. RESEARCH DESIGN AND METHODS: Twelve patients participated in the study. The 1st week of the study, all of them were on intensive insulin treatment and from day 8, four were randomized to a control group continuing with insulin, and eight to a treatment group where GLP-1 was given at meals together with regular insulin from day 8 to 12. On days 13 and 14, they were only given GLP-1 at meals. NPH insulin at bedtime was given throughout the study. RESULTS: In the GLP-1-treated patients, the doses of regular insulin, given to keep a satisfactory blood glucose control, were reduced compared with treatment with insulin only. GLP-1 virtually inhibited the early increase in blood glucose after the meals, whereas an increase of approximately 2 mmol was seen during an optimized insulin treatment. In agreement with the short half-life of the peptide, 2-h postprandial plasma insulin levels were significantly decreased both at day 12 and 14, suggesting that there was not enough GLP-1 left to stimulate endogenous insulin release and compensate for the decrease in the dose of exogenous insulin. Therefore, the effect of GLP-1 was lost before the next meal, resulting in increased preprandial blood glucose values at lunch and dinner. The concentration of VLDL triglycerides decreased already during the 1st week. This decrease persisted during the 2nd week when GLP-1 was included in the treatment. No changes were observed in the levels of LDL and HDL cholesterol. The LDL particle diameter increased from a mean of 22.1 to 22.6 nm ($P < 0.01$) in response to insulin treatment. A further increment to 22.9 nm ($P < 0.05$) was seen after GLP-1 treatment. The LDL particle size did not change in the control group. Lipoprotein lipase activity was decreased by 27% and hepatic lipase was reduced by 13% in the GLP-1-treated group. CONCLUSIONS: We confirm the antidiabetogenic effect of GLP-1 in NIDDM patients. This effect was maintained during 7 days, which implies that the patients did not develop tolerance during this treatment period. Intensive insulin treatment, leading to normotriglyceridemia, increased the mean LDL particle diameter, which is likely to lower the risk of future coronary heart disease in patients with NIDDM. Furthermore, an additive effect

of GLP-1 is indicated. Hence, this study gives additional evidence that GLP-1 may be useful as an agent for treating NIDDM.

Publication Types:
Clinical Trial
Randomized Controlled Trial

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21: Atherosclerosis 1996 Apr 5;121(2):267-73

High plasma insulin is associated with lower LDL cholesterol in elderly individuals.

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To investigate possible relationships between plasma low density lipoprotein (LDL) cholesterol and fasting plasma insulin in the elderly, cross-sectional random samples of age cohorts (65, 75, 80 and 85 years, n = 1188, M/F 38/62 percent) were studied in the neighbouring cities of Helsinki and Vantaa, Finland. Plasma total and high density lipoprotein (HDL) cholesterol, plasma triglycerides, blood glucose and plasma insulin were measured after an overnight fast. LDL cholesterol was calculated using the Friedewald equation. Statistical analyses were performed separately in subjects with non-insulin-dependent diabetes mellitus (NIDDM, n = 219) and non-diabetic subjects (n = 969). Comparison of lipid levels by insulin quartile (I < 7.4 IU/l, II 7.4-10.0, III 10.1-15.0, IV > 15.0) showed that total and LDL cholesterol decreased in the highest insulin quartile (P = 0.003). This trend prevailed after adjustments for age, gender, body mass index, blood glucose and serum triglycerides, and it was significant also in normotriglyceridemic (serum triglycerides <2.3 mmol/l) subjects. Furthermore, the association between high insulin and lower cholesterol was seen in normoglycemic (fasting blood glucose <6.7 mmol/l) and diabetic subjects. Lower LDL cholesterol in elderly subjects with higher fasting insulin may reflect poor health or a 'harvesting' effect, but the results may also be due to effects of insulin on LDL catabolism and/or cholesterol absorption.

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22: Ann Biol Clin (Paris) 1995;53(10-11):557-60

Deterioration of the plasma lipid profile during hospitalization of aged non-insulin-dependent diabetic patients. Comparison with non-diabetic control patients.

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This study aimed at investigating the changes occurring in the plasma lipid profile of patients with non-insulin-dependent diabetes mellitus (NIDDM) hospitalized for treatment of intercurrent diseases. Twenty-nine non-insulin requiring NIDDM patients (13 men, 16 women; mean age: 67 +/- 2 yrs) and 26 adequately matched patients (12 men, 14 women; mean age: 71 +/- 2 yrs) have been prospectively studied. They were all hospitalized for treatment of various diseases. Diabetic and non-diabetic patients received similar treatment except for intensive insulin therapy in the former group. On admission, diabetic

subjects had significantly higher plasma levels of triglycerides and lower levels of HDL cholesterol; during hospitalization, LDL, HDL cholesterol and apo AI levels increased significantly. In the non-diabetic group, hospitalization and treatment induced significant increases in triglycerides, LDL cholesterol and apo B levels. In conclusion, although insulin treatment during hospitalization of non-insulin requiring NIDDM patients does not fully reverse the abnormal lipid profile, it may help to prevent its further deterioration, particularly by increasing HDL cholesterol levels and hence by decreasing the LDL/HDL cholesterol ratio.

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23: Diabetes Care 1993 Apr;16(4):984-92

Effects of gemfibrozil on low-density lipoprotein particle size, density distribution, and composition in patients with type II diabetes.

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OBJECTIVE--To study the effects of gemfibrozil treatment on LDL particle size, density distribution, and composition in NIDDM patients. RESEARCH DESIGN AND METHODS--We performed LDL analyses on 16 NIDDM patients with stable glycemic control. They were randomly allocated to receive either gemfibrozil (n = 8) or a placebo (n = 8) for 3 mo in a double-blind study. The LDL particle size distribution and the particle diameter of the major LDL peak were measured with nondenaturing polyacrylamide gradient gel electrophoresis. The density distribution and composition of LDL were determined with the density gradient ultracentrifugation method. RESULTS--In the gemfibrozil group the mean serum TG concentration decreased by 38%, HDL cholesterol concentration increased by 10%, and LDL cholesterol concentration by 17% ($P < 0.05$). During gemfibrozil therapy the mean particle diameter of the major LDL peak increased from 244 to 251 A ($P < 0.05$), whereas in the placebo group the mean LDL particle diameter remained unchanged. We found an inverse correlation between the changes of serum TG and the particle diameters of the major LDL peak ($r = 0.95$, $P < 0.01$). Gemfibrozil produced a shift in the LDL density distribution toward lower density. The mean peak density decreased from 1.0371 to 1.0345 g/ml because of a significant rise in the light LDL concentration from 141.0 to 183.2 mg/dl ($P < 0.05$), whereas the concentration of dense LDL had a tendency to decrease. In the placebo group the LDL density distribution did not change. Gemfibrozil increased the CE-to-TG ratio in LDL core lipids by 27% ($P < 0.05$); otherwise, the LDL composition was only slightly affected. CONCLUSIONS--The results indicate gemfibrozil-induced changes in LDL properties in NIDDM patients are similar to those previously reported in nondiabetic individuals and are related to changes in serum TG level.

Publication Types:
Clinical Trial
Randomized Controlled Trial

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